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PROBLEMS IN THE PHYSIOLOGY OF VISUAL ACUITY

FRANCIS HEED ADLER, M.D.
PHILADELPHIA

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Visual Acuity as Measured by the Snellen Charts

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It is a matter of practical interest to inquire in detail into the various functions of the retina which are being tested in this procedure, and it is the purpose in this paper to review these functions in the light of present physiologic knowledge.

The retina provides three sensations, i. e., the light sense, the color sense and the form sense.

THE LIGHT SENSE

The light sense is the faculty of perceiving light and recognizing gradations in its intensity. It is the fundamental response of the retina to changes in its adequate stimulus, light. Although two other sensations are recognized, i. e., the color and the form sense, these are in reality merely modifications and elaborations of the light sense.

From the Departments of Physiology and Ophthalmology, University of Pennsylvania.

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(*a*) *The Minimum Visible.*—When no light falls on the retina it is in a state of physiologic rest, and its end-organs, the rods and cones, are sending no impulses up the optic nerve. If light is gradually admitted to the eye in increasing intensity, a point will be reached where the intensity of the light falling on the end-organs is sufficient to stimulate some of them, and they will send a discharge or burst of impulses up the optic nerve. These impulses are recognized as the familiar action currents found in all sensory and motor nerves.

No impulses are discharged until a certain threshold is reached, as each end-organ requires a certain amount of light energy to set it off. It is possible to attain this total quantity of energy, within certain limits, either by increasing the intensity of the light or by prolonging the time of the exposure. A beam of light which is so faint that it fails to stimulate when an exposure of 0.05 second is given may be effective when an exposure of 0.1 second is allowed. Only those cones will be discharged whose threshold of stimulation has been reached.

It has been assumed by certain investigators, notably Hecht, that the cones in any one section of the retina do not all have the same threshold of stimulation, but that some discharge at light of low intensities, while others discharge only when the intensity has been considerably increased. There is no direct evidence that this is the case, however, and it may be that all of the end-organs in any one region have the same threshold and all discharge when that threshold is reached.

The threshold value of the light sense is termed the minimum visible. It is different for various regions of the retina and varies enormously in those regions with the state of adaptation of the eye. When the eye is completely dark-adapted the perimacular region is the most sensitive to light of low intensities, whereas under these conditions the fovea itself is practically a blind spot. When the eye is light-adapted, on the other hand, the fovea is much more sensitive to slight changes in illumination than is the periphery. These facts are well known and need not be considered here.

It is important to recognize that the perception of light depends on the quantity of light energy which reaches the receptors and on their minimum visible, and has nothing to do with the size of the stimulus on the retina. A small bright stimulus may be just as effective as a large faint one, and the result will be determined by the total quantity of energy presented to the receptors. The minimum visible cannot be defined, therefore, in terms of visual angle. This fact is well illustrated by the visibility of the stars. The visual angle which each star subtends at the eye must be very small, and its visibility depends solely on the intensity of light which reaches the retina.

The photochemical processes which take place in the rods and cones and which ultimately lead to the discharge of a nervous impulse are not as yet sufficiently known to warrant a discussion in this paper.

(*b*) *Influence of Aberrations in the Refractive System of the Eye on the Minimum Visible.*—If the eye were a perfect optical instrument, a small point of light, such as light from a star, would be focused on the retina as a small point image. In physiologic optics one is accustomed to speak of "object points" and of "image points" and to visualize the image of a luminous point on the retina as a point image. This conception is so firmly established that it is usually taken for granted that an image point can be limited to the area of a single cone in the fovea. It has even been assumed that image points can be so sharply focused that only a portion of a cone can be stimulated, and that not only is the center cone in the fovea the most sensitive percipient element but there is a spot in this cone which is more sensitive than the surrounding portions and which may be regarded as the point of true fixation.

It is probable, however, that the image of a point can never be limited to the area of a single foveal cone, much less to a restricted area within the diameter of a cone. Even an eye which is strictly emmetropic suffers sufficiently from aberrations to prevent an ideal image formation such as was postulated. Because of irradiation the image of an object point is never a true point on the retina, even though monochromatic light is used. Every point image on the retina is a small diffusion circle (taking the form of the pupillary aperture), and the intensity of light in this circle is not evenly diffused but is maximum at the center and gradually fades off toward the periphery. Hartridge's calculations may be cited as an illustration of the probable amount of spreading of a point image on the retina. He assumed that in the case of a narrow bright line on a dark background, the pupillary diameter being 3 mm., the intensity of the light on the row of foveal cones which exactly corresponds to the center of the image of the line equals 100. If the diameter of the foveal cones is 3.2 microns, he calculated that the intensity of illumination on the rows of cones which lie on either side of the central row is 31 per cent; that the next row of cones is illuminated by 9 per cent, and so on. Not until the sixth row of cones is reached has the intensity of illumination fallen to as low as 1 per cent. "In other words, even in the case of the image of a linear source, a large number of retinal cone elements receive stimulation, and it is not possible to think of any one cone or even any one small group of cones as being alone stimulated."

Figure 1 shows the distribution on the retina of light intensity from a single source of light. In the figure *ad* represents the surface of the retina (rod and cone layer). Perpendiculars erected on this plane represent the intensity of light falling on the surface. If there were no optical imperfections in the eye, the surface from *A* to *B* would be equally illuminated, and the intensity of illumination would be measured

by the height of *AD* and *BC*. The total illumination of the surface between *A* and *B* would then be represented by the figure *ABCD*.

Because of the spread of light owing to the optical imperfections in every eye, the actual area of the retina which is stimulated is larger than that formed by the visual angle of the entering light. How much larger this stimulated area actually is will depend on the threshold of light sense of the underlying cones, i. e., their minimum visible. The total illumination of the surface will actually be represented by the figure *abcd*. A point of light entering the eye will probably form a diffusion circle larger than a cone itself if it is intense enough to stimulate a single cone. Although a number of cones may be covered by the image, only a few may actually be discharged, depending on their threshold.

One can say, therefore, that since an image point probably cannot be limited in size to the diameter of a foveal cone, it is useless to look for thresholds of the light sense in terms of visual angles limited by the size of the foveal cones. This is the experience of all investigators,

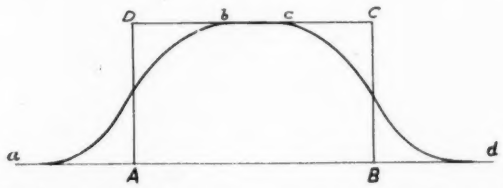

Fig. 1.—Distribution of light intensity on the retina from a single source.

who agree that the minimum visible of structures such as fine black threads on a white background is not limited in any way to the size of the foveal cones but is determined solely by the capacity of the retina to distinguish between two degrees of brightness. Einthoven [1] found that such threads could be clearly seen even though they subtended an angle of only 2 seconds.

(c) *Influence of Sensory Adaptation on the Minimum Visible.*—Every sensory end-organ in the body will discharge an impulse only as long as it is being stimulated, and a stimulus is a change in the environment. In order to have continuous excitation, the environment must be continually changing or fresh end-organs must be constantly affected by the stimulus. If the stimulus remains constant and no fresh end-organs are called into play, the state of excitation soon dies down and no impulse is sent up the nerve. If one plunges the hand into hot water the heat spots in the skin are stimulated and send up a sensation of warmth. If the hand is kept in the water this sensation of heat soon dies away, although the temperature of the water may not have changed

1. Einthoven: Arch. f. d. ges. Physiol. **191**:60, 1921.

at all. In order to have a further sensation of heat, the temperature of the water must be increased a certain amount, and within a certain period, or the hand must be plunged farther into the water so that fresh heat spots are stimulated.

This dying down of the impulse from sensory receptors is called sensory adaptation. It is a property of the rods and cones and affects the light sense of the retina to a large degree.

It is obvious that a light source which is sufficient to stimulate a certain cone or group of cones in the retina soon loses its effect unless it changes in brightness or unless new cones are being continually brought under its influence. A light source which is so feeble that it is just at the threshold of perception will soon fall below the minimum visible if it remains fixed on a small group of rods and cones. The eye protects itself against this effect of sensory adaptation by never remaining still. Even during the most exact fixation the eye probably undergoes small movements which constantly carry a small point source of light over a number of end-organs. The nature and extent of these ocular movements will be considered in more detail in a later paper. They have been well described by a number of writers and are thought to consist of relatively large excursions of about 4 minutes of arc, occurring at intervals of 1 second, and between these are fine oscillations, the extent of which has not been so thoroughly measured. It is possible that the eyes do not fixate the same way for all purposes, and it is a mistake to assume that because a test object is so small that it subtends an angle of less than 1 cone diameter its image is in reality limited to stimulating a single cone. During fixation of the test object the eye may have so moved that the image is carried over a large number of elements.

(d) Gradations of the Light Sense with Changes in Intensity.—König calculated that the eye could perceive about 660 steps in brightness in the range of intensities perceptible to the eye. Hecht suggested that these steps represent the addition of more functioning elements. As the intensity of a stimulating light is increased, each distinguishable increase in brightness represents the addition of one new functional element per unit area. It is possible, however, as Wilcox and Purdy[2] pointed out, that a change in the number of functional receptors is not required to explain the steps in discrimination of brightness, but that the factor responsible is the way in which each individual cone responds to altered stimulation.

Adrian and Mathews showed that there is an increased frequency of the impulses in the optic nerve with increasing intensity of stimulation. This means that each receptor responds to an increase in light intensity

2. Wilcox and Purdy: Brit. J. M. Psychol. **23**:233, 1933.

by discharging more impulses. It is yet to be learned within what limits a single receptor can change the number of impulses it discharges, and whether these account satisfactorily for the known number of steps in discrimination of intensity. The conception of each receptor modifying the nerve impulse with a change in the intensity of the stimulus seems contrary to the old belief in the "all or none" law as applied to all sensory receptors.

THE COLOR SENSE

The color sense is a modification of the light sense in that one is enabled to discriminate between the different wavelengths of the spectrum. Since it has no bearing on the present problem it needs no further discussion.

THE FORM SENSE

The form sense is the ability to discriminate a contour. It is the faculty by which one perceives the shape of objects, and it depends on the ability of the retina to distinguish between excitation and non-

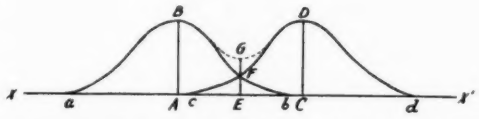

Fig. 2.—Diagram illustrating the intensity of light energy falling on the retina when two points are stimulated.

excitation. It is therefore a higher development of the light sense and necessitates a retina which is capable of sending to the brain information regarding different degrees of stimulation.

(*a*) *The Minimum Separable.*—One of the most elemental examples of the form sense is the discrimination of two points as separate points. The same processes are concerned here that were outlined for the light sense. The only additional feature is that there must be an unstimulated cone or group of cones lying between the ones which are stimulated. Figure 2 is a diagram illustrating the intensity of light energy falling on the retina under these conditions. When the object points are close together the intensity of the light at the point *E* may be above the minimum visible for the underlying cones, and so only the sensation of a line is recorded. Only when the object points are moved far enough apart so that the intensity of the light at the point *E* falls below the minimum visible will there be a sensation of two separate points.

An analogy may be drawn between the minimum separable and the ability to detect two points of contact on the skin. If a pointed instrument is applied to the skin over a touch spot a sensation is aroused as soon as the pressure applied exceeds the threshold of the touch spot.

If two such points, for instance, the ends of a divider, are applied to the skin, a sensation of two points of contact will occur only when the points stimulate two separate touch spots. If the touch spots are relatively few, as they are in the skin of the back, the dividers may have to be widely separated before the sensation of two distinct points can be made out. On the other hand, in a region of the body where the touch spots are numerous, such as the tips of the fingers, the arms of the divider may be very close together and still give the sensation of two separate points of contact. In this sensation, therefore, the important factor for the discrimination of two points is the distribution of the end-organs in the skin. Where they are numerous there will be fine discrimination, and where they are sparse the discrimination will be relatively coarse.

This is also true of the retina. In a region where the end-organs are closely packed together the discrimination of two points as separate, i. e., the minimum separable, should be very fine, whereas in a region where the end-organs are sparsely distributed the discrimination should not be as acute. This is found to be true. This sense not only is highly developed in the fovea, where the cones are closely packed together, but is almost limited to this region. The threshold for the minimum separable is very low in the light-adapted fovea, and within from 3 to 5 degrees increases to almost double. From this point outward the threshold increases gradually.

There is another reason why the periphery of the retina is so inferior to the fovea in the minimum separable. The threshold will be limited in part by the aberrations present in the optical media, and these are much more pronounced in the periphery than in the center of the eye. Fineness of perception demands that the image be as sharply focused on the retina as possible so that the contour will be sharp and the differentiation between stimulated and unstimulated cones as abrupt as possible. All refractive errors, by causing larger diffusion circles on the retina, prevent this fine discrimination. In this respect the form sense differs slightly from the light sense, as tested by the minimum visible. The threshold of the light sense is determined entirely by the sensitivity of the rods and cones. There need be no sharp border between stimulated and unstimulated end-organs, which is the essential factor in creating a contour, and hence optical defects or cloudy media do not interfere with this function to nearly the same degree as with the form sense. The light sense remains normal in the presence of a cataract up to the stage of maturity, and any significant change should be regarded with suspicion as indicating a damaged retina or optic nerve. When there is blood in the aqueous or vitreous, on the other hand, the light sense is considerably reduced. This is due to the dispersion and diffraction of the light by each individual corpuscle, so that the amount

of light which finally reaches the retina falls below the threshold of the rods and cones. When there is blood in the vitreous all perception of light may be lost, but after absorption of the hemorrhage good vision may return.

Since any diminution in sharpness of the retinal image lowers the minimum separable, this test or one of its modifications will be useful in determining the refractive power of the eye. The Landolt broken ring test falls under this category, since one is required to orientate the break in a ring in respect to its position in the ring. If the whole background of the test card were black and the subject were required to tell the appearance of a spot of white the test would be a measure of the minimum visible, but since each black ring is surrounded by white one is dealing with a circle of unstimulated retina, in some portion of which lies a spot equaling in intensity the stimulation of the whole retina. Locating this spot in the ring constitutes discrimination of the two ends

TABLE 1.—*Measurements of the Minimum Separable*

Observer	Value at Retina in Microns	Angle in Seconds
Lister	4.6	64
Hirschmann	3.6	50
Bergmann	3.8	52
Helmholtz	4.6	64
Uhthoff	4.0	56
Cobb	4.6	64

of the unstimulated portion, and the separation of these ends from one another makes this discrimination easier, just as separating two dots makes their detection as two separate dots easier.

(*b*) *Measurements of the Minimum Separable.*—The minimum visual angle under which two points can be resolved by the normal human eye has been investigated by a number of observers. Table 1 gives the figures found by various investigators.

In the past, considerable emphasis has been placed on the fact that the threshold for the minimum separable corresponds to a distance on the retina occupied by the diameter of a foveal cone. It seemed logical to conclude from this that the minimum separable is determined by the size of the foveal cones. The size of the foveal cones, as found by a number of workers, is given in table 2.

The average value for the minimum separable is approximately 4 microns, whereas the average diameter of the foveal cones is approximately 3.5 microns, which is a fairly close correspondence. Wilcox and Purdy pointed out that the value for the minimum separable exceeds the diameter of the foveal cones by a sufficient amount for one to say that this threshold is probably determined by the size of the cones.

No one, as they correctly stated, has given threshold values for the minimum separable which are smaller than the size of a foveal cone. It is probably useless, however, to try to base the limits of this function on the anatomic size of the cones, as the methods used in the histologic preparation of sections of the retina must have a considerable effect in altering their size. Gordon Walls,[3] who has been attempting for some time to secure superior preservation of the visual cells in sections of fresh normal human eyes, in a personal communication wrote as follows:

> The diameter which foveal cones will exhibit in preserved and sectioned material is so largely dependent upon the excellence of the technique that I feel that we will never know that diameter within one-half a micron until an entirely normal head is perfused first with Ringer-Locke at body temperature and then with a supreme retinal fixative also at body temperature; this ideal procedure has not been possible. . . . Too much attention has been given to the diameter of cone outer segments by those who use such data in working out the morphological limit of visual acuity, for the curvature of the shoulder of the human cone inner segment is so gentle that it would be impossible for light which enters it radially at any point in its cross-sectional area to escape laterally; thus all the light which enters the inner segment is gathered into the base of the outer segment, and the diameter of the latter and the distance on center between adjacent cone outer segments are meaningless figures.

TABLE 2.—*Size of the Foveal Cones*

Observer	Diameter in Microns
Schultze	2.8
Müller	3.0
Merkel	3.0
Wadsworth	2.5
Kühne	2.0-2.5
von Kölliker	4.5-5.4
Koster	4.4
Grief	2.5
Dimmer	3.0-3.5

It is true, therefore, that the threshold and the size of the cones correspond, but this may be merely coincidence, and it will be seen in the next section that this correspondence does not hold in all examples of the form sense.

(*c*) *The Alining Power of the Eye.*—If the acuity of the eye is tested by determining the smallest break which can be detected in the contour of a straight line, the threshold values obtained are surprisingly small. A good observer can tell a break in a straight line when the break subtends a visual angle of only 10 seconds at the eye, and under optimal conditions figures as low as 2 seconds have been reported.

3. Walls, Gordon: Preliminary Note on the Form of Human Visual Cells, Arch. Ophth. **4**:106 (July) 1930.

The alining power of the eye is the essential factor in the discrimination of a contour and is therefore of importance in visual acuity as tested with letter charts. This sense has been described in the literature under many different names, which sometimes creates considerable confusion. Duke-Elder [4] spoke of it as the "minimum distinguishable change of contour." Other writers have called it the "displacement threshold," or the "vernier threshold," and Hering carefully distinguished between this sense and the minimum separable by speaking of the former as the "Raumsinn," or sense of space, and of the latter as the "Auflösungsvermögen," or resolving power of the eye.

It is generally agreed that displacements in a line can be detected when the shift in the image on the retina is much smaller than the diameter of a cone, and this has occasioned many theories as to how

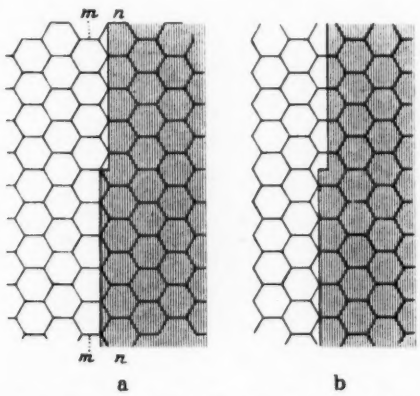

Fig. 3.—Diagram showing the break in the line as lying between two rows of cones.

the retina can have such fine discrimination. In the case of the minimum separable the limits of acuity correspond well with the best measurements of the diameters of the foveal cones, and this agrees with the idea that acuity is determined by the fineness of grain of the sensory end-organs. But it is evident that this is impossible in the case of the alining power of the eye.

Hering and Best tried to explain the situation by picturing the break in the line as lying between two rows of cones, as illustrated in figure 3. If this conception is correct, the threshold of the alining power should vary as the test object is turned in space so that its image lies on different meridians of the retina. It is claimed that this is not the case, however, the threshold remaining the same whether the line is in the vertical, horizontal or oblique positions in space.

4. Duke-Elder, W. S.: Text Book of Ophthalmology, London, Henry Kimpton, 1932, vol. 1, p. 922.

An explanation which, although more complex, probably represents the actual facts better is that proposed by Weymouth and Anderson.[5] They based their theory on the scattered arrangement of the cones as depicted by von Fritsch.[6] In his illustrations the cones are not arranged in exact hexagonal rows, closely packed together, but show a considerable scattering with interspaces between them. Hence the retinal image of a straight contour would not be received by a regular and unbroken row of cones. Since one has the impression of a straight line, and not a broken one, a smoothing-out, or averaging, process must take place among the "local signs" of each cone in the irregular row. The final percept of the line is obtained by the average or mean local sign of the row.

Anderson and Weymouth pointed out that the eye is in constant motion even during the most exact fixation, so that the image of the line must be swept over a large number of cones, and since the accuracy of a percept depends on the number of cones stimulated the movements of the eye will enable one to obtain an extremely accurate perception of any displacement in a part of the line. According to these authors, this idea is confirmed by the fact that the threshold for the alining power is dependent in some degree on the length of the lines of the test object and on the fact that if the effect of ocular movements is prevented by giving very short exposures to the test object, the threshold values increase considerably. All these facts point to an increase in the number of cones stimulated as being the important factor in the very low thresholds that are found for the alining power of the eye. This is not confirmed, however, by the investigations of French,[7] who found that the alining power was very little affected by changes in the illumination. If one agrees with Hecht that the increase in the acuity tested by the minimum separable with increasing illumination is due to the larger number of cones called into activity, one would expect to find the alining power of the eye increased similarly.

(*d*) *Differences Between the Minimum Separable and the Alining Power of the Eye.*—It is evident from the foregoing statements that these two retinal functions are very different from one another in their threshold values and that they are affected differently by changes in experimental conditions. The alining power of the eye is probably four times as sensitive as the minimum separable. It is said to be a function of the length of the test lines used and to vary with the time of exposure given, i. e., whether the effect of the constant ocular move-

5. Weymouth and Anderson: Am. J. Physiol. **64**:561, 1923.

6. von Fritsch: Ueber Bau und Bedeutung der Area centralis der Menschen, Berlin, G. Reimer, 1908.

7. French: Tr. Ophth. Soc. U. Kingdom **21**:127, 1920.

ments during fixation is present or not. Changes in illumination do not affect the threshold. No studies have been made on the threshold values for different regions of the retina, such as have been made for the minimum separable.

The minimum separable, on the other hand, has a threshold so nearly of the same order as the size of the foveal cones that it suggests a dependence of one on the other. This could be true only if the eyes were absolutely still for at least a fraction of the time taken to fixate any object, so that the image could rest on an exact pattern of foveal cones and not be swept over a large number of elements. The threshold is found to vary with the illumination in a characteristic fashion, and the threshold varies enormously with the portion of the retina used for fixation.

As Wilcox and Purdy pointed out, the minimum separable depends on the perception of a difference in brightness between two contours and their interspace, and in this respect there is no difference between the minimum separable and the minimum visible save one of complexity. The alining power of the eye, on the other hand, probably does not depend so directly on the perception of brightness but is determined by some other mechanism. This may be in part retinal and in part a function of higher centers.

No satisfactory data can be found in the literature comparing the threshold of the minimum visible with that of the alining power of the eye when the eye suffers from refractive errors. It is not known whether a condition of ametropia affects the minimum visible and the alining power equally. Similarly, it is not known whether a disease of the retina or of the optic nerve influences these two thresholds equally.

VISUAL ACUITY AS MEASURED BY THE SNELLEN CHARTS

Visual acuity as measured by means of the Snellen test charts is not a test of retinal activity alone but includes many other physiologic and psychologic functions. The ability to read test type involves the power of attention, the motor coordination of the eye, directing it to fixate accurately on the letter to be read, familiarity with test type and other psychophysiologic factors. Hence, reading a chart of test letters involves many functions which, when harmonized, yield a percept. A perceptual pattern is recognized only so far as it has meaning. The letter A inverted can have no meaning of A until the subject realizes its inverted position. It will instinctively be called a V, for an intelligent person will know that a letter consisting of two limbs forming an acute angle with the apex above can only be a letter A, whereas one similarly formed having its apex below can only be a V.

The test that is used for visual acuity, therefore, is a test of many functions besides those of the retina. It is employed clinically for two

main purposes, although these are not always clearly distinguished from one another by this test. It is used to detect defects in the optical system of the eye, i. e., to measure ametropia, and it is also used to detect any impairment in the functions of the retina. From a practical point of view the reading of letters may be the best method to use in working out the refractive error of a patient. It has the advantage in providing a natural stimulus to the subject to make small discriminations, and in spite of the fact that it is relatively a crude test it probably is adequate for the purpose.

As a means of testing impairment of the retina the reading of letters is undoubtedly inadequate, and its shortcomings have long been realized. As Traquair emphasized, a patient may have vision of 6/6 and still have a central scotoma for very small white or colored test objects. A circumscribed area of retinochoroiditis just outside the macula will seldom affect the visual acuity of an eye unless the media are cloudy, and one is often surprised to find lesions scattered throughout the macula in patients with normal visual acuity. I have under my care now a patient with advanced optic atrophy which followed the injudicious use of tryparsamide, whose visual fields are constricted to within 1 or 2 degrees of fixation (as close to the fixation point as can be measured by a tangent screen) and yet the visual acuity is 6/6 in each eye. The central foveal cones and their conducting fibers have escaped the damage. In spite of this normal central acuity the patient has to be led around as though he were totally blind.

Slight changes in the function of the retina or optic nerves are not demonstrable with the usual visual acuity test, and it is possible that some other method which makes use of finer discrimination might be devised for those cases in which it is needed.

The Snellen test letter charts were made so that each letter would subtend an angle of 5 minutes and each part of each letter an angle of 1 minute at the eye. This was done with the erroneous idea that the visibility of a contour, such as a letter, was limited by a normal threshold of 1 minute. The discrimination of a letter has little to do with the minimum separable but is largely a matter of the alining power of the eye. It should be clearly understood that there is no good physiologic reason for making the letters this customary size, and that the practice is continued merely as a habit.

SUMMARY

All of the functions of the retina, no matter how elaborate, are fundamentally based on the faculty of perceiving light, i. e., the light sense. The liminal stimulus for the perception of light depends on the threshold of stimulation of the rods and cones. Although this ultimately depends on the total quantity of light energy falling on the retinal

receptor, it is influenced to a large degree by many factors, such as spatial and temporal induction and sensory adaptation.

The threshold of the light sense is termed the minimum visible. It cannot be measured in terms of visual angle, but only in units of light energy.

The minimum separable, i. e., the ability to discriminate two separate points, is similar in all respects to the minimum visible except that its threshold value can be expressed in terms of visual angle, since an unstimulated cone or group of cones must lie between the ones stimulated. It is possible that the close correspondence between the threshold of the minimum separable and the known size of the foveal cones is merely coincidence, since it is doubtful if the images on the retina can ever be limited in actual extent to the diameter of a cone. It is possible that they may be limited functionally, however, in that the light which is spread over adjoining cones falls below the threshold of stimulation. In any event, the threshold values of the minimum separable have never been found less than the diameter of the foveal cones. Both the minimum visible and the minimum separable depend on a difference in brightness.

The alining power of the eye is the ability to detect a slight change in a contour, and depends not on perception of brightness alone but on other unknown factors. It is possible that this sense, which is far more acute than the minimum separable, is mediated by an averaging process whereby a large number of retinal elements are stimulated. Further studies should be made to compare the alining power with the minimum separable, especially to note if the type of fixation of the eye is different during the two types of discrimination.

Visual acuity, as tested with the Snellen charts, is not a test of the various retinal functions alone but involves many other physiologic and psychologic factors. The discrimination of a letter is not a test of the minimum separable alone but involves the alining power of the eye. It is erroneous, therefore, to regard the 1 minute standard which was set for the size of each part of the letter as having a physiologic basis. The alining power of the eye is far more sensitive than this, and actual practice shows that contours, such as letters, can be discriminated by the normal eye when they subtend a visual angle of much less than 1 minute.

In practice, the letter charts are probably the best test for working out the refractive condition of an eye, but they can undoubtedly be improved if a test of retinal function alone is desired. The extent and severity of a lesion in the fovea cannot be measured accurately, and its progress cannot be satisfactorily recorded, with the present crude methods. There are already in the literature evidences of dissatisfaction with the reading of letters as a quantitative measure of retinal function. This will probably result in the development in the near future of tests which analyze more closely the physiologic functions of the retina alone.

BILATERAL GLIOMA TREATED BY RADIUM

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Radium and roentgen treatment of ocular conditions has been added to the armamentarium of ophthalmologists and used for various ocular diseases since the early years of this century. The main conditions which have been treated at various times and places are: eczema of the lid, blepharitis and other dermatologic entities about the eye; carcinoma; chronic conjunctivitis; trachoma; follicular catarrh; vernal catarrh; pterygium, nevi and angiomas; acute as well as chronic dacrocystitis, with some success, especially in the tuberculous types; ulcus serpens; marantic corneal ulcers; herpes of the cornea and keratitis parenchymatosa, as well as disciform keratitis; scleritis and sympathetic ophthalmia; epithelial cysts of the iris; hemorrhages in the vitreous of juvenile patients and angiomatosis of the retina; glaucoma; myopia and opacities of the vitreous, and lastly, coming to the subject of primary interest in this paper, intra-ocular tumors, especially gliomas.

It can readily be seen that practically no plausible ocular condition has escaped a trial of treatment with radium or roentgen rays. Among the list, however, there are only a few conditions in which, during the last thirty years of trial, treatment by radium or roentgen rays has become a well established procedure. For epibulbar carcinoma, sarcoma of the lid, nevus and tuberculous dacrocystitis these forms of treatment are often those of election. For all the other conditions mentioned they are of little or no value, and when cases reported by incompetent observers are eliminated, the election of radium and roentgen therapy is restricted to a very small field. Because of their desperate nature, cases of intra-ocular tumor with glioma involving both eyes stand out as being of greatest importance in this field.

Under what conditions is one justified in choosing or advising one of the two methods of treatment in these cases? The first method is that of enucleation with subsequent irradiation of the orbital contents; the second, direct irradiation of the intra-ocular tumor without enucleation. In the presence of one unaffected eye with useful vision, enucleation of the affected eye is always to be chosen. Thus, the cases in which irradiation is to be considered are either those in which there is bilateral tumor, or those in which the tumor is in the only useful eye and that eye still retains some vision. Even here, the patient, or the parents of the patient, must be told of the incomparably greater danger to life in

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the case of radiation as compared with enucleation of the only useful eye, and consequently permanent blindness. It is not often in practice that one is confronted with this choice. The occasions are practically confined to those of bilateral glioma and of sarcoma of the choroid in the only useful eye. To these may finally be added the rare cases of metastatic carcinoma of the choroid, usually arising from cancer of the breast and, as in a recent case of mine, occurring as late as five years after removal of the primary growth. Roentgenograms will often show multiple small metastases of the cranial bones, and death is likely to occur within a short period of time; so that, unless such an eye is painful, enucleation may not be called for, and roentgen or radium therapy may deter the intra-ocular metastatic growth from progressing.

In reviewing the literature, it seems that no cases of choroidal sarcoma have ever resulted in a cure. A transient regression of the growth was obtained by Parker and Stokes, and by Janeway in three cases with, however, subsequent growth. Birch-Hirschfeld, with combined radium and roentgen treatment, obtained a regression of the sarcoma in the only eye of a 29 year old patient with, however, injury to the lens, and after three years the eye had to be enucleated because of a painful secondary glaucoma. Microscopically, there was an extensive regression of the growth, but there still remained small areas of well stained and active tumor cells. In no cases of malignant choroiditic tumors has a cure followed; enucleation was never avoided. On the other hand, a diminution of the tumor occurred in one instance, and in some cases enucleation was postponed for several years. In general, the results of the treatment of so-called glioma of the retina have scarcely been more favorable, although there are a few well established cases of maintenance of eyesight and life for several years and one case which, judged from the standpoint of the so-called five year cure, can bear that analysis. This case, that of a child whose left eye was enucleated in 1923, was reported by Paul Knapp and Ludin. Thirteen months after enucleation a small glioma was seen in the right eye. One year after treatment the tumor was smaller, and two years later it was still smaller, but there was a disciform, posterior, cortical cataract. In 1927, the child was still alive and in good health. The condition was the same in 1929, but there was a fully developed cataract. After repeated discissions, the vision with glasses was 7/10. The fundus showed a large, old choroiditic area of atrophy. There is no question regarding the accuracy of these observations. I shall later mention some cases in which a cure was claimed but follow-up later showed that the patient eventually succumbed. Other cases were not observed from two to three years after treatment, and their fate is not known. One may suppose, however, that they belong to the great number of cases in which the tumor finally destroyed both eye and life, for in a dissertation of Sticherling of the Freiburg

Eye Clinic in 1927, forty-three cases of glioma were reported in which radium, roentgen rays or a combination of these forms of therapy was used with supposed cures in only three cases. Since then Jensen reported other cases in which there are two possible cures; one was a case of Marzio's—a bilateral glioma in a child of 4 months, who was treated at intervals of one month. Six months after treatment the right eye was enucleated. Microscopically, it showed a total detachment of the retina but no gliomatous elements. The left eye showed a flat choroidal scar one and one-half years after treatment, with the child recognizing small objects, although the lower half of the visual field was lacking. One of Fleisher's patients was treated from January, 1927, to June, 1928. There were four gliomatous nodules, of which two were scarified and the others showed positive regression at the end of the first year. The patient was still being treated at the time the case was reported, but that was four years ago and I do not know the final outcome. Odinzov enucleated one eye and treated the second eye over two years. It then became distinctly worse and was enucleated. Jensen enucleated a left eye for glioma in 1926, the right eye being normal. In 1928, the parents noticed a change in this remaining eye. It then showed a glioma in the macular region. Treatments were carried on for a year, there being in general a slow but definite regression with occasional fresh outbursts. In 1929, the tumor was growing toward the optic nerve. The patient then escaped observation, but in 1931 the mother wrote that the vision was almost gone, that the eye was pressed forward between the lids, that bloody fluid was present and that the child was emaciated.

So far one lesson is definitely to be emphasized: It is not enough to examine both eyes, establish the absence of a glioma in the non-affected eye and call the case one of one-sided glioma. In two cases mentioned so far I have seen a tumor develop in the normal fellow eye in from one to two years. I should therefore insist, in one-sided cases, on keeping in touch with the patient as regards fairly frequent ophthalmic examinations of the remaining eye for at least two or three years before the case can definitely be declared to be only one-sided.

Axenfeld, in 1914, published the report of the first case of glioma in which radium therapy was used. The case was broadcast, naturally, through the ophthalmic literature. A cure was believed to have been established for some time, and the case is still referred to frequently as one in which a cure was obtained. It is to Axenfeld's credit that this whole subject was first taken up with interest and future cases of bilateral glioma were given the benefit of radium treatment; his original case, however, did not result in a cure. The cilia and eyebrows were destroyed; cataract developed two years later, followed by detachment of the retina, corneal ulcer, perforation and enucleation.

In 1921, Axenfeld published another case, that of a 6 year old girl who three years before had had the right orbit exenterated for glioma. There was at that time a circumscribed scar of a probably spontaneously reabsorbed glioma in the left eye. Two years later a fresh glioma appeared in this eye. Retinal detachment developed after treatment; the prognosis was given as uncertain to say the least. Axenfeld remarked on the curiousness of spontaneous healing of a glioma followed by a second nodule in the same eye. Incidentally, while a great rarity, the spontaneous disappearance of a gliomatous nodule is well authenticated. It would be too much to say that the few cures obtained by radium and roentgen therapy have been only a curious juxtaposition of treatment of a glioma and a spontaneous cure; very captious critics might take that point of view.

In order to give some illustrative examples of the course of treatment in cases which temporarily appeared to be cured and in those in which no result was obtained, the following résumé of some of the cases in the literature is appended:

REPORT OF CASES

CASE 1 (F. H. Verhoeff).—*Glioma of the Retina Treated by Roentgen Rays.*

An infant, aged 17 months, on Nov. 24, 1917, had the right eye removed. The right orbit was given five severe roentgen treatments. On May 2, 1918, in the lower quadrant of the other eye there was a mass of 4 papilla diameters; nearby were two small white spots one-fourth papilla diameter in size. A suberythema dose was given through a 5 mm. aluminum filter once a week for three weeks, and on five subsequent days from June 6 to June 17, 1918. On Oct. 19, 1919, the tumor appeared less translucent, smaller and less elevated; the white spots disappeared. On June 18, 1921, below the center of the tumor was a circular depressed area about one-third papilla diameter in size and slightly pink in contrast to the rest of the tumor. The vision was estimated at 20/30 by testing with pictures. The lens was protected by filtering through a lead plate.

CASE 2 (K. Kusama).—*Roentgen Treatment of Retinal Glioma.*

An infant, aged 1 year and 2 months, was treated for one year and seven months, being exposed to the roentgen rays ninety-three times. The quantity of irradiation was 645.5 Holzknecht units, 617 being applied to the right eye and 584.5 to the left eye. Each application was made from the front of the eye for from five to ten minutes. The focal skin distance was 20 cm.; the hardness of tube from four to seven w;[1] the thickness of the aluminum filter, from 1.5 to 30 mm. The total dose of roentgen rays was from 5 to 8 Holzknecht units each time. The eyelids were inflamed; the eyelashes fell out; the cornea became hazy, and hyphemia and phthisis bulbi developed. Death occurred in eighteen months from metastasis to the brain.

CASE 3 (K. Kusama).—*Roentgen Treatment of Retinal Glioma.*

An infant, aged 6 months, seen on April 14, 1917, died on March 12, 1918. The changes were the same as in the foregoing case. There was a metastatic tumor in

1. "From four to seven w" refers to a type of tube in use a number of years ago.

the frontal, right temporal and parotid regions, under the abdominal wall and in the inguinal region. The patient died in a debilitated condition. Roentgen therapy was applied to each eye forty-six times, the right eye receiving 296.5 Holzknecht units and the left eye 311.5 Holzknecht units; 120 units was applied ten times to the nodules in the right parotid region. Radium was applied to each eye thirty times, one hour at a time.

CASE 4 (K. Kusama).—*Roentgen Treatment of Retinal Glioma.*

An infant, aged 5 months, seen on Jan. 28, 1916, died on April 14, 1918. Metastases to the cranium, dura, liver and pancreas occurred. The right eyeball was proptosed by the tumor in the orbit. Shrinking of the tumor in the eye took place after a few exposures to the roentgen rays. Phthisis bulbi developed within seven months in this case and within two years in case 2.

CASE 5 (Arnold Knapp).—*Bilateral Glioma Unsuccessfully Treated with Radium.*

A boy, aged 6½ years, was seen on April 28, 1919. On Nov. 4, 1914, the left eye was removed because of a glioma; there was an extensive glioma on the right eye. On May 12, 1919, 414 millicuries of radium filtered by 2 mm. of lead and 0.5 mm. of silver was applied for five hours at a distance of 2 cm. from the skin over the right temple. There was improvement for six weeks; then the active area above the disk became enlarged and swollen. One June 23, 168 millicuries was applied with the same filtration at a distance of 2.5 cm. for fifteen hours. On July 31, 1,312 millicuries was applied with the same filtration but over a larger area at the side of the orbit at a distance of 3 cm. for two and a half hours. On October 6, 1,227 millicuries in a smaller container but with the same filtration was applied at a distance of 3 cm. to the side of the orbit for two hours. There was no improvement, and the eye was subsequently enucleated.

CASE 6 (Arnold Knapp).—*Retinal Glioma Treated with Radium.*

In a child, aged 11 months, the left eye, which showed extension of the disease into the nerve, was enucleated; the right eye had a moderate-sized glioma. On April 17, 1920, 30 mg. of radium was applied to the right eye and the left orbit. The lids were sealed with adhesive, and the radium was held in place with adhesive strips. Eight hours was the duration of each application; the radium was screened with 1.4 mm. of gold and 12 mm. of gum rubber. There was no reaction. On April 28, 50 mg. of radium was applied with a marked reaction; the outline of the radium container was seen over both orbits. The lids were edematous. On June 7, the tumor was no larger. On July 12, the growth was flatter but the same in extent.

CASE 7 (Mark J. Schoenberg).—*Bilteral Glioma of the Retina Apparently Arrested in the Nonenucleated Eye by Radium Treatment.*

The left eye of the patient was enucleated. On April 10, 1916, radium emanations of 36 millicuries with a lead filter were applied to the right temple for four hours. On September 22, the patient received 58 millicuries filtered through a 4 sq. cm. lead plaque held over the eye at a distance of 1 cm. for eight hours; on June 7, 209 millicuries filtered through lead plaques, 2 and 0.5 mm. thick, held over the right side of the orbit for fourteen and a half hours. On September 30, the posterior portion of the lens near the pole showed opacities. On December 5, there was an irregular lobulated area, very slightly raised and extremely white. The mass was surrounded by patches of choroidal atrophy. In June, 1919, it appeared the same.

These cases will serve sufficiently well as illustrations of the methods and usual results in the application of radium external to the eye or of roentgen treatment.

Next to be considered are the cases in which radium is inserted as close to the tumor as possible. I refer to those reported by Moore, Stallard and Milner and by McDowall and Marks, résumés of which are given here. Radon seeds were inserted in such a fashion that the seed was not visible on ophthalmoscopic examination. The authors succeeded only twice with this method. They localized the tumors as one localizes retinal tears. The seed was kept in the eye for ten days. A rubber shield was placed on it in some cases; the seed was lost in the vitreous in one case. Except for a reaction of the outer parts of the

Fig. 1.—Glioma of the retina.

eye, which was not excessive, there was little evidence of intra-ocular reaction; the hemorrhage was small.

Case 8 (Moore, Stallard and Milner).—On Nov. 15, 1929, a 3 millicurie seed was used. On December 3, the mass was smaller. A hole was seen at the point of insertion of the seed. On July 8, 1930, a 5.3 millicurie needle was inserted through the old hole. This seed slipped into the vitreous. On March 13, 1931, there seemed to be a recurrence. On March 29, four seeds of 3.5 millicuries were applied to the sclera in such a way that the hole was in the center of them. The seeds were sewn into the sclera and left in for ten days. The patient is still under observation. Changes are occurring in the optic disk, and sight has deteriorated.

Case 9 (Moore, Stallard and Milner).—The eye was enucleated after ten days' exposure to 3.5 millicurie seeds inserted in the growth. Grossly, there were no changes in the tumor; on section, marked degenerative changes were seen in the vicinity of the radon seeds. They were also present throughout the tumor. All the vessels in the uveal tract and optic nerve were congested.

Case 10 (Moore, Stallard and Milner).—On Sept. 23, 1930, two 4.8 millicurie seeds were inserted in the growth. Grossly, there was no alteration in the cream cheese appearance. One part of the growth appeared to be increasing, and on Jan. 21, 1931, a 3.5 millicurie seed was inserted. Panophthalmitis developed.

Case 11 (Moore, Stallard and Milner).—Both eyes were full of tumor. The child died on the operating table. Examination of the eye showed that a seed could be placed at a point 1.5 mm. from the disk. The retinal glioma was treated by the insertion of small radium needles in the orbit.

Case 12 (McDowall and Marks).—A child, 6 months of age, had a bilateral glioma. One eye was enucleated. The mass in the upper temporal quadrant was

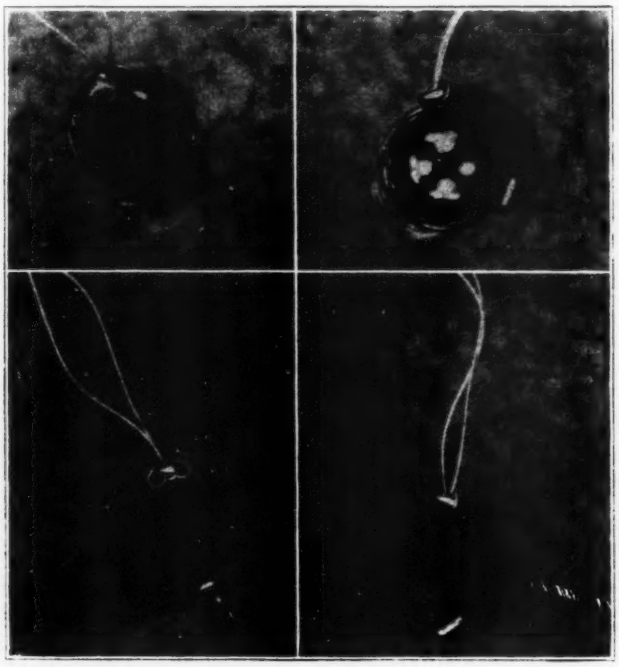

Fig. 2.—Protheses containing radium needles.

elevated 11 diopters. The diameter of the tumor was about two thirds of the distance between the macula and the anterior limit of vision with the dilated pupil. The tumor just missed the macula and was well away from the optic nerve. On June 12, three needles of 0.5 mg. and 0.5 cm. in length were inserted through small openings in the upper lid over the area nearest the base of the tumor and were placed 1 cm. apart. They were removed after six days. A total dosage of 216 mg. hours was applied. There was slight reddening of the skin about the incision, but no inflammatory reaction in the eye. On June 29, the mass was irregular, shrunken and elevated 4 diopters. On July 20, there was an irregular, patchy white area, elevated 1 diopter. From August 7 to 9, radium treatment was applied through a Columbia paste mold (yellow wax and sawdust), 2 cm. in thickness, to the upper part of the orbit and right temporal regions by means of 4 mg. needles, of 2 cm. active length and filtered with 0.5 mm. of platinum. The total dosage was 960 mg. hours. On May 27, 1932, the condition remained the same as on July 20, 1931. The tumor was markedly affected by treatment.

From an analysis of the other cases in the literature, however, this does not mean that there may not be fresh nodules forming under intense treatment, or that there may not be a quiescent period with fresh tumor formation after several years. The knowledge, however, that Foster Moore had inserted radon seeds into the tumor itself induced me to employ this treatment in the following case:

A 1 year old child was brought to the Standard University Eye Clinic on Sept. 13, 1932. The diagnosis was bilateral glioma. The right eye, which was completely filled with a tumor mass, was enucleated, and histologic examination confirmed the diagnosis. The left eye showed a gray-white mass of about 5 papilla diameters, with sharply circumscribed edges and an elevation of from 3 to 4 diopters, located slightly above the horizontal meridian and adjacent but not in contact with the optic nerve, as seen in figure 1. The retinal vessels passed

Fig. 3.—Roentgenogram of the orbit showing radium needles.

over the mass. Several deep vessels not related to the retinal vessels passing over the mass were observed in the body of the tumor; otherwise there were no abnormal changes in the fundus. The child was too small for the estimation of any accurate vision, but acted as a child with normal vision would. The treatment consisted of two 5 mg. needles in a wax mold (fig. 2), slipped as far back along the curvature of the eyeball as possible by detaching the external rectus muscle and cutting through the capsule of Tenon. The location of these needles can be well seen in the roentgenogram taken of the orbital region (fig. 3). As regards the dosage, if the needles were point sources the maximum intensity would have been equivalent to 400 mg. hours at 1 cm., but, as a matter of fact they were elongated so that the maximum intensity was somewhat less. This mold was in situ for twenty-four hours and was then removed by means of a small wire thread, which had been left projecting from the external incision. This irradiation took place on September 21. When the patient was examined on October 27, under gas, the tumor was of the same elevation and size as originally described, but an exudate with some pigment deposit had formed about the lower and temporal edges of the tumor which showed two small areas of necrosis. On December 15, the original tumor appeared as on previous examinations, but in the nasal superior retinal quadrant was seen another mass about the size of the nerve head and

circular, with sharply marked edges. On December 28, radium was again inserted as on the first occasion. On this occasion Dr. Robert Newell gave the following description: "Insertion of needles again about 14 mm. apart directed backward, that approach to about 1.5 to 2 mm. of the eyeball at the centers. Were they point sources the intensity would be 2,500 mg. hours at 1 cm. At center of free surface of tumor it would be about 310 mg. hours at 1 cm. Considering how well the eyeball stood the September treatment, I think this dose will not destroy the sight. Time, 20 hours."

After this the baby was seen repeatedly, and on examination under gas on April 6, 1933, the condition was as shown in figure 4. The site of the original tumor was occupied by a wavy detached retina, our impression being that there was

Fig. 4.—Fundus following radiation.

no solid mass beneath it. At the lower edge of the detachment, however, were tumor masses which I think represented an extension downward of the original growth, although a well marked walling off in the direction of their extension by the area of pigmentation was seen. The second tumor in the nasal superior quadrant was, while not regressive, certainly not progressive. The general picture, however, leads one to consider further treatment both by the method used and possibly by a combination of this method and a cross-fire application of roentgen rays.

Examination on September 15, showed, however, that the detachment was larger downward, taking in the area which represented an extension of the mass downward. The small new nodule, shown in figure 4, had disappeared, leaving behind a yellow area with obliterated choroidal vessels and sprinkled with fine black pigment. The lower edge of the detachment was outlined by a fresh striate retinal hemorrhage. In short, neither the main tumor mass nor the fresh nodules were to be seen. The child had gained 10 pounds (4.5 Kg.) in weight over the last year, and seemed to see as much and acted as normally as before.

On November 2, the left eye was enucleated. The child had not been seen for a month, but two weeks preceding the enucleation, the mother noticed that the child was fretful and rubbed its eye and that there was loss of vision. On examination it was found that there were extensive retinal detachment, fresh tumor masses and slightly increased tension.

We have, therefore, not proceeded with the treatment, feeling that processes of destruction may have reached the optimum and that processes of repair are still taking place; the latter are of great importance and may effectually check the general metastasis and wall off any remaining active tumor cells.

All tissues can be destroyed by large doses, whereas small doses may have no effect. It seems proved that the rays attack the cellular nucleus, and it is probable that the cells are especially susceptible to them during division. What chemical substance the rays affect is not as yet known. Some believe that it is the colloidal proteins; other that the effect of the rays rests on an activation of ferments; others that the point of attack is the lecithin; others that the rays work through physical means, as for instance, a small point of heat, which causes the coagulation of the proteins. It is certain that different tissues prove themselves different in their reactions. One can divide the tissues into those that are extremely susceptible, those that are more than usually susceptible, those that are susceptible and those that fall below a certain threshold of susceptibility. Depending on these factors, especially in the case of ocular tissue, precaution has to be taken as regards excessive radiation. Experiments on animals by Birch-Hirschfeld as long ago as 1904, and recently by Lane in America, show that all grades of ocular damage can result. Dermatitis with loss of the lashes and eyebrows, purulent conjunctivitis, interstitial keratitis, sclerosis of the walls of the vessels, degenerative changes of the ganglion cells of the retina and an ascending secondary optic atrophy, and, finally the formation of cataract. The last-mentioned condition may occur years after the exposure. The useful dosage is not definitely ascertained; with the variability of the resistance of tissues and especially with the variation in the resistance of the tumor mass, depending somewhat on its age, size, kind and unknown factors of biologic qualities, the dosage can never be accurately standardized. The art of the physician, after all, consists in grading the dose according to the effects obtained with the definite and yet indefinable factor of judgment which one man may possess and another man may never obtain.

The Gifford Edwards prize essay for 1932 by H. B. Stallard entitled "Radiant Energy as a Pathogenic and as a Therapeutic Agent in Ophthalmic Disorders," published by the *British Journal of Ophthalmology* as a monograph supplement, has recently been received by the medical library at Stanford University. For those desiring more details

of case reports and an accurate statistical survey of the malignant tumors of the eye of all kinds treated by radium or roentgen rays, it is a valuable publication. The literature on glioma of the retina, sarcoma of the choroid and the harmful effects of radium listed at the conclusion of this paper is cited on pages 78 and 79 of the prize essay.

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EXCISION OF CORNEAL LEUKOMA

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Excision of the anterior layers of the cornea can be accomplished with comparative safety when the eye is free from inflammation. It is a satisfactory method for removal of unsightly leukomas, multiple foreign bodies superficially buried, pseudopterygium, painful corneal scars that frequently break down and result in recurrent ulcers and degenerating anterior layers of cornea in certain types of dystrophy. The results of the operation are frequently gratifying from the visual and cosmetic standpoints. The cornea, however, always remains partly cloudy after the excision of the anterior layers, and visual acuity, at best, is impaired.

New corneal epithelium grows rapidly. After excision of the anterior layers to within 2 mm. of the limbus, the entire cornea will be recovered with epithelium in from four to seven days. Regeneration of the substantia propria occurs much more slowly, but under favorable conditions excised tissue may be entirely replaced. In an eye that has been free from inflammation for several months, the regeneration of the cornea takes place with little reaction and practically no discomfort. Corneas that are very vascular, as in interstitial keratitis, or that have been perforated so that scar tissue extends through all of the layers are not suitable for resection, as the resulting scar usually is more dense than that before operation.

In order to study the regeneration of corneal tissue, a series of experiments on rabbits' eyes was carried out by Rucker.[1] With the rabbit under ether anesthesia, the superficial layers of the cornea were excised by making a circular incision of from 1 to 2 mm. within the limbus through about two thirds of the thickness of the cornea and then peeling off the central disk. Various means of protecting the denuded cornea were tried. Attempts made to protect the regenerating cornea by covering it with a flap of bulbar conjunctiva tied with purse-string sutures were failures. The subconjunctival tissue became adherent to the corneal stroma within a few days, preventing growth of the epithelium. The conjunctiva was swollen and congested as a result of the trauma produced by such an extensive operative procedure.

From the Section on Ophthalmology, the Mayo Clinic.

1. Rucker, C. W.: Regeneration of the Cornea, Arch. Ophth. **2**:692 (Dec.) 1929.

Closure of the lids by sutures did not affect the early growth of the epithelium, but when the lids were left closed for more than five days the corneas became badly infected.

Conditions were less complicated when eyes of human beings were operated on, as there was no question of cleanliness, and infection was seldom to be found. Conjunctival flaps were not used, nor was it necessary to unite the margins of the lid. The cornea was covered with a modified mercuric chloride ointment, and a common gauze and cotton dressing was applied. In no case was there serious infection. The reaction was negligible, and the eyes were comfortable.

In order to determine the best means of obtaining optimum visual results, several methods of removing the desired amount of cornea were tried. For instance, when only the lower half of the cornea was leukomatous, should it alone be removed, or should the entire cornea be uncovered? Would new epithelium grow from the limbus alone or from the cut edge over the center of the cornea as well? Should the incision be beveled or right-angled? If regeneration of the epithelium and substantia propria proceeds uninterruptedly, uncovering of the entire cornea would seem to be preferable if the central margin of the leukoma is situated in the pupillary area. The shoulder, even though made with a rather long bevel, forms a considerable ridge, producing optical distortion greatest at that line and troublesome in proportion to the relative clearness of the inner and the outer sections of the cornea.

Progress of the growth of epithelium may be observed by instillation of potassium fluorescein, the intensity of the stain and the area affected by it being noted. New epithelium was observed to grow out from all margins, and the growth from the cut edge near the center of the cornea was as rapid as that from the edge near the limbus, so that the last area to be covered was at the center of the denuded area. Here there was often some delay in uniting the advancing edges caused by overriding, brushing by the lid, floating on fluid or merely lack of complete union. In time, however, all the areas were entirely covered with new epithelium.

OPERATION

In some cases, incisions were made across the cornea at right angles, bisecting it in two meridians. The cornea was then resected in quadrants, beginning at the points at which the incisions crossed. The center of the cornea yields to slight pressure so that it is difficult to resect all four quadrants in the same plane. Consequently, small remnants of corneal tissue remained over the pupillary area. For the removal of extensive leukomas, the method practiced by Rucker in his experiments on animals proved to be more satisfactory.

Resection of large, quadrilateral areas is the most satisfactory method from the standpoint of ease of operation, as well as of visual results. The horizontal sides are slightly longer than the vertical, the corners of the area to be resected touching the limbus at points corresponding to 2, 4, 8 and 10 on the dial of a clock. Under local anesthesia, the section to be removed should be circumscribed by beveled incisions made with a sharp corneal scalpel through three fourths of the thickness of the cornea. Beginning at one corner, one may then remove the whole section in one piece by following the line of cleavage in the cornea and by cutting with the belly of the scalpel.

REPORT OF CASES

According to the indications for operation, the cases here reported are divided into four groups, according to the presence of (1) congenital leukoma, (2) multiple foreign bodies, (3) scars from burns and (4) recurrent corneal ulcers.

Group 1: Congenital Leukoma.—CASE 1.—A woman, aged 22, had congenital opacities of the cornea, ptosis and nystagmus. Vision in each eye was reduced to ability to count fingers. The corneas were normal in size and the epithelium smooth; the central portions of the corneas were almost white, and the peripheral zones, which were from 2 to 3 mm. wide, were light gray. The area of dense opacity was slightly smaller in the left eye. By transillumination the corneas appeared to be translucent, and the peripheral portions were sufficiently transparent to permit a view of the iris and the pupillary border. The irides appeared to be normal, and the pupils reacted to light. Intra-ocular tension was normal.

The corneal leukoma in the right eye was excised on Jan. 26, 1923. Crucial incisions were made vertically and horizontally over the center of the cornea through three fourths of its thickness. The four segments of the cornea were dissected up and cut off near the limbus. When the leukomatous portion had been removed, the pupil and iris could easily be seen through the center of the thin cornea, which appeared to be clear.

The entire cornea became epithelized within five days. The reaction was slight. A 10 per cent solution of ethylmorphine hydrochloride, U. S. P., was instilled once daily from the time the patient was dismissed from the hospital. There was no appreciable improvement in vision during the first year. During the next three years, the cornea became considerably clearer, but in the central area an opacity remained because the dissection had not been carried out in the same plane. In September, 1925, by beginning at one side, the central opacity was resected in one plane. Following the operation, the cornea was much clearer; details of the structure of the iris could be made out, and two years later the patient was able to get about with vision of the right eye only. Because of rapid nystagmus, a satisfactory view of the fundus was not obtained. Undoubtedly, some other optical defect was present.

Group 2: Multiple Foreign Bodies Superficially Buried in the Cornea.—CASE 2.—A man, aged 32, was injured on Feb. 6, 1928, by the explosion of a high-pressure gasoline still. The right eye was badly lacerated and was removed fourteen days later. Fine particles of steel were blown into the face so that the skin was blackened, and looked as if it had been burned with black powder. The bulbar conjunc-

tiva and cornea of the left eye in the palpebral fissure were filled with black particles of steel dust. The cornea was not perforated, and the pupil reacted to light. The lid was swollen shut for several weeks, and the cornea became infected. On July 4, when the patient appeared at the clinic, the eye was painful, the lids were swollen and the conjunctiva was chemotic, but the cornea was only superficially affected.

A large rectangular section of the cornea with a large number of foreign bodies was resected on July 9. The reaction following the operation was mild, although the bulbar conjunctiva was swollen and congested. By July 24, the reaction had subsided. The cornea became vascularized from the nasal side, leading to a thin leukoma, 3 mm. in diameter, at the center of the cornea. Vision equaled 2/60. Peripheral vision, however, gradually increased so that in October the patient could get about alone, see well enough to play cards and read large headlines in the newspaper. On May 3, 1929, vision with sphere + 1.00, combined with a cylinder + 1.0, axis 180, equaled 6/60, and the patient was able to drive a truck, which he did regularly for several months.

CASE 3.—A man, aged 39, came to the clinic on Dec. 10, 1931, because of a large leukoma of the left cornea caused by a hot cinder three years previously. Vision of the right eye was 6/6, and that of the left eye, 2/60. The leukoma was sharply circumscribed, 5 mm. in diameter and situated at the center of the cornea, leaving the periphery clear except for a leash of vessels at 1 and at 5 o'clock.

The leukoma was resected on the day of admission, December 10, in a large quadrilateral section, two-thirds the thickness of the cornea. Healing was prompt and uneventful. Two months later, the cornea was cloudy but did not stain with fluorescein. Vision was not improved to more than 2/60. The cosmetic result, however, was satisfactory.

CASE 4.—A man, aged 22, entered the clinic on Oct. 27, 1925. At 5 years of age, the left eye had been injured. One year later, a scar which gradually increased in density appeared over the center of the cornea. The patient could see large letters with this eye until two years previous to presentation. On the day of admission, vision of the right eye was 6/4-2; that of the left eye, ability to count fingers at about 18 inches (46 cm.). The left cornea contained a dense central opacity, 6 mm. in diameter. On the nasal margin of the opacity was a cream-colored leukoma which reached almost to the limbus. This area had developed during the last two years. Otherwise the periphery of the cornea was clear.

On October 28, the anterior three fourths of the cornea was resected in a large, quadrilateral flap. As the resection was finished, the cornea was perforated, and the aqueous humor escaped. Two days later, the chamber had reformed, and in nine days, the entire cornea was recovered with epithelium. Atropine and ethylmorphine hydrochloride were instilled daily after the operation. The eye remained red for three months. Except for occasional periods of irritation, the eye was free from injection afterward. On June 2, 1930, vision equaled 2/60. There was a nebulous opacity, 5 by 6 mm., slightly discolored brown. The cornea appeared to be of normal thickness, and the defect was scarcely noticeable.

CASE 5.—A man, aged 51, came to the clinic on June 3, 1929, because of blindness caused by an explosion of dynamite three and a half years previously. The vision was reduced to perception of light. In the right cornea, there was a dense scar involving all but a crescentic area, 2 mm. in width in the upper portion and a similar area at the lower border. The left cornea was opaque and covered by a pannus extending upward from the base of an ectatic mass at the lower border of the cornea to the center. The ectasia below involved the iris and the ciliary body.

On the day of admission, a quadrangular section composed of three fourths of the thickness of the cornea was resected; this included the leukoma but left a clear zone more than 2 mm. in width above and below it. The posterior portion of the cornea was found to be vascular and opaque. On July 10, the cornea was covered with epithelium, and the patient was dismissed without having received any benefit from the operation.

CASE 6.—A man, aged 41, came to the clinic on June 1, 1931. His eyes had been injured in an explosion of dynamite twenty months previously. The left eye was removed shortly afterward. He had perception of light only in the right eye, although an optical iridectomy had been done in the superior nasal quadrant. Examination revealed considerable foreign substance in the bulbar conjunctiva and a dense corneal scar in the central and inferior portions.

On June 4, the anterior layers of the upper portion of the cornea were removed so as to uncover the coloboma. The lower portion of the cornea, including the leukoma, was not removed because of its vascularity. Details of the iris could be made out through the remaining layers of the cornea, and the patient remarked immediately that his vision was clearer. As the epithelium regenerated, the cornea became more cloudy. On June 16, the lower portion of the cornea, including more layers of the upper portion, was resected, but the entire scar was not removed. Vision was improved. On June 23, the patient was able to count fingers temporally, and the upper portion of the cornea remained fairly clear. This slight improvement in vision was of considerable help.

Group 3: Burns.—CASE 7.—A woman, aged 23, came to the clinic on Aug. 15, 1932. Vision of the right eye was 6/6; she could see moving objects with the left eye. When she was 6 years of age, she was burned over the left side of the face by slacked lime. The palpebral and ocular conjunctivae were thickened, and some scarring resulted in the shallowing of the lower culdesac and in the formation of one rather dense band of adhesions from the culdesac to the limbus, on the nasal side. The cornea was covered with a roughened, vascularized, white scar, through which it was rather difficult to discern the color and markings of the iris. The patient wanted the scar removed for cosmetic improvement.

On Aug. 16, the anterior three fourths of the cornea was removed to within 2 mm. of the limbus, and the entire leukomatous area was excised in one piece. Six days later, epithelium had regenerated so that the cornea did not stain with fluorescein. The reaction was not severe, but the eye was sensitive to light and to wind, which occasioned troublesome epiphora. The regenerated cornea, however, was so much clearer that the patient was satisfied with the result of the operation from the cosmetic standpoint.

CASE 8.—A man, aged 44, was injured on June 7, 1926, by concentrated lye. He was examined at the clinic on May 7, 1929. In the right eye, there was perception of light. The left eye had been removed. The conjunctiva of the right eye was scarred and extended down over the cornea. There was a scar across the central portion of the cornea, with a small bit of clear cornea between the two scarred areas.

On May 17, a skin-muscle operation was performed for entropion, and the upper portion of the cornea was excised. The patient was dismissed from observation on May 23, with the upper portion of the cornea healed and clearer than before operation. I have been unable to obtain further information concerning the patient.

Group 4: Leukoma from Recurrent Corneal Ulcers.—CASE 9.—A man, aged 45, came to the clinic on May 21, 1929. The vision in each eye was reduced to seeing moving objects at about 1 foot (30 cm.). The patient had suffered recurring

attacks of corneal ulceration since childhood. The last attack previous to his coming to the clinic occurred in March in the left eye. In April, the right eye became involved. Vision gradually diminished as photophobia and pain increased. Examination of the right eye showed the bulbar conjunctiva thickened throughout, especially near the limbus. The cornea exhibited marked infiltration that extended inward from the limbus for several millimeters, leaving a less infiltrated area (3 by 5 mm.) in the center of the cornea that stained with fluorescein. The left cornea also was markedly infiltrated on the temporal side, and a band, 3 mm. in width and extending from 12 to 5 o'clock, stained deeply with fluorescein.

Foreign protein and local treatment were instituted. On September 9, 1930, the patient returned with dense scars over the corneas. The vision of the right eye was 6/60 and of the left 1/60. The central portion of the left cornea was cloudy, with an amber tint in the central portion of the scar. There were no calcareous deposits, but diffuse cloudiness of the cornea, involving only the anterior layers, was present. On September 9, a section of the cornea extending from the nasal to the temporal margins was removed, leaving about 3 mm. of cornea above and below. On September 23, the cornea was much clearer than before operation, and vision had improved to 2/60.

The patient returned to the clinic on Oct. 20, 1932. The vision of the right eye was 3/50; that of the left, 6/30. The patient had used ethylmorphine hydrochloride in the left eye for two years. He felt that vision had been greatly helped by the operation, and he requested that a similar operation be performed on the right eye. Examination of the right eye revealed diffuse cloudiness in the lower two thirds of the cornea, which was rather superficial and spotted. In the left eye, there was some cloudiness of the lower portion of the cornea, with a small, nebulous opacity on the temporal side of the anterior pole. The cornea was smooth and covered with glistening epithelium and showed no deformity from the operation.

Operation was performed October 21. A border of 3 mm. was left above, and the remainder of the anterior layers of the cornea were removed to the limbus. By October 29, the cornea was epithelized and did not stain. On March 13, 1933, the patient reported by letter that the visual result had not been so good as he had anticipated.

Case 10.—A boy, aged 9 years, was seen on July 16, 1919. Three years previously he had a severe inflammation in the left eye, which resulted in cloudy vision and congestion without pain. Within a few weeks, the vision of the eye was reduced to the perception of light. Six months later, a cataract in the eye was needled. During the next year, three more needlings were performed. In January, similar inflammation occurred in the left eye. On examination, the right globe was found to be normal in size and free from inflammation. There was a central area of redness, 4 mm. in diameter, in the cornea, just below the anterior pole, which by oblique light was seen to be composed of a large number of highly refractile bodies situated anteriorly in the cornea. In the left eye, there was a similar but much denser haze of the cornea. The patient was not seen again at the clinic until September, 1926. Vision of the right eye was 4/60, with correction. The eye was free from inflammation. The lower two thirds of the cornea was hazy, and just below the anterior pole was a small, white plaque. The upper third of the cornea was clear.

On October 5, the opaque portion of the left cornea was resected and excised at the limbus. The clear portion of the cornea was not removed. Four days later, the cornea had become epithelized. There was no cloudiness of the cornea

except a thin line above the center, where part of the cornea was not removed. On October 11, the right eye was operated on to remove the horizontal band of opacities. The patient was dismissed on November 11; the eye was free from inflammation and the corneas were slightly rough, with no signs of recurrence of opacity in the resected areas. Vision was poor because of slight cloudiness of the corneas and heavy vitreous opacities in both eyes.

CASE 11.—A woman, aged 24, came to the clinic on June 25, 1924, because of an unsightly scar on the right cornea. A corneal ulcer during an attack of measles had resulted in a scar when she was 2 years of age. Vision of the right eye was 6/60 (eccentric); that of the left, 6/5 with glasses. In the right cornea was a dense, white scar, roughly oval and measuring 5 by 7 mm.; it was situated at the lower edge of the cornea. Above this was a roughly triangular area of less dense corneal infiltration. Both areas were superficially visualized. The balance of the cornea was diffusely hazy. Intra-ocular tension was 32 mm. of mercury.

On June 27, the leukoma near the limbus was excised. It was thick and did not all come away. On July 5, the cornea was covered with epithelium, but there were a few small vessels in the corneal stroma. Two days later, a considerable portion of the epithelium had been abraded so that a third of the resected area stained with fluorescein. On July 19, the cornea had not quite healed. Vascularity near the limbus was increased, the opacity became thicker, and it was evident that there was no benefit to be derived from the operation. On May 8, 1929, five years later, there was considerable bulging of the cornea in the region from which the scar had been removed. Enucleation was advised.

CASE 12.—A woman, aged 53, was seen in the clinic on July 10, 1928. Since the age of 5, she had had ulcers of the cornea of the left eye, recurring at intervals of from eight to ten years, and she had never been able to read with this eye. The right eye became inflamed on March 17, 1927. The cornea probably was ulcerated, although the patient was not sure of it. Within a week, vision of this eye was practically lost, and the eye did not recover from the inflammation for six months. It finally healed with a large central leukoma. In the right eye was a large leukoma over the central portion of the cornea, leaving a border of clear cornea, 3 mm. in width, entirely around it. There was a brownish, granular deposit in the deeper layers of the cornea, and the scar was vascularized from the temporal side. Vision was reduced to the ability to note moving objects. In the left eye, there was a large central leukoma, thinner than that in the right, leaving a border of clear cornea 4 mm. above, 2 mm. below and 3 mm. on each side. There were small vessels on the nasal side. Vision in this eye equaled 6/60.

On July 19, 1928, a large rectangular piece of cornea, including the central leukoma, was removed from the left eye. As the operation was finished, a pinpoint perforation occurred on the nasal side. Four days afterward, the chamber was reformed, although shallow, and the pupil was dilated. There was an anterior synechia at the site of the perforation. Two weeks later, the cornea was still slightly cloudy, but the eye was comfortable and vision without glasses was 1/60. The patient was advised to use a 5 per cent solution of ethylmorphine hydrochloride. The result of the operation may be best judged from an extract from a letter written on Nov. 23, 1929: "Look how well I write! I have tried to be so patient, but I cannot yet read, but I want you to know that I consider the operation you performed on my eye a wonderful benefit to me. It is now over a year since the eye healed, and I suppose the improvement is about as much as it will be. My greatest confusion, aside from inability to read, comes from the

effect of auto or any electric light which blinds me. Doctor V. explains the cause being the irregularities of the cornea."

CASE 13.—A man, aged 52, came to the clinic on May 31, 1928. The vision of the right eye was 3/60; that of the left eye was ability to perceive moving objects. Two years previously, he had suffered inflammation in both eyes, which lasted about three weeks. When the inflammation subsided, the vision was much impaired. Six months later, the eyes again became inflamed and painful. After a few weeks, the inflammation subsided without medication. On the right eye, there was a dense, oval scar at the center of the cornea, 3 by 4 mm. in size, with the axis horizontal. The remainder of the cornea was hazy and contained small leashes of vessels extending from the limbus above, down to the scar. Intra-ocular tension was normal. On the left eye, there was a dense, granular leukoma, 7 mm. in diameter, at the center of the cornea. Around its border, the cornea was clear for less than 1 mm., and beyond this clear ring was a narrow, grayish-white ring, beyond which there was still another narrow ring of clear cornea. Slit-lamp examinations of the right eye disclosed a large central opacity in the substantia propria of the cornea, composed of interlacing white fibrils, with considerable vascularity deep in the cornea. In the left eye, the central mass was made up of heavy, cloudlike deposits and many finer arterioles.

The left eye was operated on on June 6. Crucial incisions were made, crossing up and temporally, 3 mm. from the anterior pole. The four sections were then dissected back to the limbus and cut off, leaving a very clear portion of cornea, through which the iris markings could be made out. Four days later, there was a prominent leash of vessels growing over the cornea from the nasal side toward a mass of scar tissue, 3 mm. in diameter, near the center of the cornea. The right eye was operated on on June 15. The cornea was divided into four quadrants, the largest quadrant being down and nasally. All four sections were removed to the limbus, and as deeply as possible. There was slight cloudiness of the cornea of both eyes, which was more intense toward the center, and as the tissues regenerated, the vascularity increased. On June 25, the vision of each eye was about 2/60. Slit-lamp examination after the operation revealed that the corneas were very thin, the left being thinner than the right. Small vessels extended over the whole of each cornea, growing in from the periphery. Nine months later, in response to an inquiry, the patient said he had not received any help from the operation.

CASE 14.—A woman, aged 63, was seen at the clinic on June 28, 1928. The vision of the right eye was 6/60; that of the left eye was ability to count fingers at a distance of 2 feet (60 cm.). Six years previously, the left eye had become painful, and vision declined. After several months, the pain disappeared, but vision remained poor. Four years previous to the patient's visit, both eyes had become inflamed; the condition disappeared after several months, but vision in both eyes remained poor and gradually decreased, although there had been no further attacks of inflammation. Examination disclosed irregular opacities throughout the lower two thirds of each cornea. Intra-ocular tension was normal. The diagnosis was sclerosing keratitis of both eyes, with a dense leukoma in the left eye.

On the day of admission the leukoma was excised by resection after crucial incisions. The eye healed promptly, and the cornea became epithelized, with only moderate reaction. A 10 per cent solution of ethylmorphine hydrochloride was instilled daily for several months. On August 30, the cornea had become fairly clear, and the patient could see to get about with vision of that eye alone. Over

the pupil, at the point of the crossing of the incisions, a white opacity, 1 mm. in size, obscured the vision.

CASE 15.—A man, aged 28, was seen in the clinic in July, 1924. The vision of the right eye was 6/5; that of the left was ability to count fingers at a distance of 1 foot. There was a dense scar on the left cornea, following inflammation of six months' duration, which had occurred two years previously. One year previously, a milky white opacity had developed in the outer half of the cornea of the right eye, but this did not impair central vision. Examination showed the right cornea to be clear except for a spindle-shaped scar in the temporal half, 2 mm. from the limbus and measuring 3.5 by 1.5 mm. In the left eye, there was a dense central leukoma, with a zone of less dense infiltration around it and a 3 mm. zone of clear cornea all the way around. The cornea was traversed by numerous vessels.

On July 14, the leukoma of the left eye was scarified and treated with alcohol and ether. A few years later, the patient reported that there had been considerable improvement in vision for several months after the treatment, but that vision had again failed.

CASE 16.—A man, aged 59, was seen in the clinic on Nov. 28, 1928. Vision of the right eye equaled ability to see moving objects; that of the left eye was 3/60. Twenty years previously the patient had been struck on the right eye by a chip. Ulcers occurred on both corneas and were cauterized. He was free from ulcers for fifteen years, and then the right eye was again cauterized for ulcer. In February, 1928, an ulcer of the right cornea occurred which did not heal until May. There were scars of the central corneas, 5 mm. in diameter, the scar in the right eye being more dense than that in the left. In the right eye was a dense central leukoma surrounded by a 3 mm. zone of relatively clear cornea, traversed by a few deep vessels. In the left eye, an irregular, nebulous opacity covered most of the cornea except the superior nasal quadrant. The opacity was not dense nor was it vascularized, as was the right eye. Optical iridectomy of the right eye improved the vision to 6/60.

On Dec. 29, 1929, a leukoma of the left eye was excised; this improved vision from 3/60 to 6/60. The cornea remained cloudy and slightly vascular. Vision was slightly, but not materially, improved.

CASE 17.—A man, aged 62, was seen in the clinic on Oct. 27, 1930. Vision of the right eye was ability to see moving objects; that of the left eye, 6/6+. Loss of vision in the right eye resulted from recurrent ulcers of the cornea, beginning in 1928, with a gradual increase in the density of the scar. The leukoma was situated centrally and was made up of several segments of different density. One large vessel entered the leukoma from the limbus at 1 o'clock.

On August 28, the leukoma was removed down to a very thin membrane which was still slightly cloudy. On September 13, the haziness of the cornea had practically disappeared. On March 13, 1931, the patient reported by letter: "The eye has improved to the extent that I am not disturbed by electric lights or bright sunlight. There is an occasional burning sensation. The vision is not improved."

COMMENT

Resected portions of the corneas examined microscopically disclosed fibrosis and cellular infiltration. A human eye from which a leukoma has been excised has not been examined microscopically, since none of

the eyes operated on have, to my knowledge, been removed. It is difficult to ascertain the depth of a leukoma by any method of examination, and, although it seemed that in several cases the posterior layers of the cornea were quite clear immediately following resection, they were invariably cloudy a few days later. I have not seen any improvement in the transparency of a resected cornea that could be attributed to the use of ethylmorphine hydrochloride, and I think its value for that purpose is nil.

The operation is not difficult, and there is little danger of increasing the injury to the eye. Its chief value lies in cosmetic improvement, and in suitable cases the result is of greater satisfaction to the patient than the report would seem to indicate.

CYST OF THE OPTIC NERVES AND CHIASM ASSOCIATED WITH AN EPITHELIOMA OF RATHKE'S POUCH

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History.—I. O. D., a girl, aged 12, was referred to the Memorial Hospital, Richmond, on Aug. 31, 1932, by Dr. S. P. Hileman, of Millboro, Va., because of frontal headache, progressive loss of vision, and drowsiness. Headache was first noticed six months previously, being occasional and not accompanied by nausea or vomiting; school work was continued. The school nurse found subnormal vision and advised refraction.

Glasses were fitted in June by Dr. Frank Wysor, of Clifton Forge, Va., who furnished the following notes: "My records show that I. O. D. was sent to me for refraction on May 31, 1932, and that her vision at that time was 20/40. Under atropine cycloplegia her error was found to be + 0.75 sphere with + 0.75 cylinder axis 90 degrees in each eye, and vision was improved to 20/30 plus. Nothing pathologic was noted in the fundi. No check-up of the visual fields was made."

Six weeks before admission to the hospital the headache became severe and constant and vision worse, but varied greatly from time to time. Drowsiness was noted three weeks before, and the child, previously very alert, slept a good deal of the time. The temperature was slightly elevated. Diplopia was acknowledged, but apparently she had not been distressed by it. The past and family histories were essentially unimportant. The child had lost 13 pounds (5.9 Kg.) in the past two months. There were occasional attacks of tinnitus.

Examination.—Physical examination showed nothing abnormal except rather large pupils and pale nerve heads. Vision varied from ability to count fingers to 10/200 in each eye. The visual fields were entirely unsatisfactory. The right disk appeared more atrophic than the left. There was no choking, and no new tissue was seen over the disks. If a papilledema had been present it had entirely disappeared, leaving no traces. The picture suggested a primary atrophy (E. H.).

Except for drowsiness, the cerebral functions were intact and the reflexes all normal. A roentgenogram of the skull showed no pathologic process; the pituitary fossa was normal (Dr. D. D. Talley). On September 6, the lateral ventricles were punctured, and a small amount of air was injected. A roentgenogram showed small ventricles and no shifting of the lateral ventricles.

On September 12, because the ventriculogram was not entirely satisfactory, injection of air was made into the lumbar region (130 cc. of fluid removed and 130 cc. of air injected). The roentgenographic report was as follows: "The lateral ventricles appeared normal and not shifted in position. The third ventricle was unusually well delineated, large and crescentic in shape, with convexity upward,

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the floor being concave. The foramina of Monro appeared quite large. No cortical atrophy was seen. The shape and appearance of the third ventricle were unusual, and this was considered suggestive of pressure from below, which might be due to a new growth" (Dr. D. D. Talley).

Fig. 1.—Encephalogram showing the dilated third ventricle (upper arrow) and the location of the tumor (lower arrow).

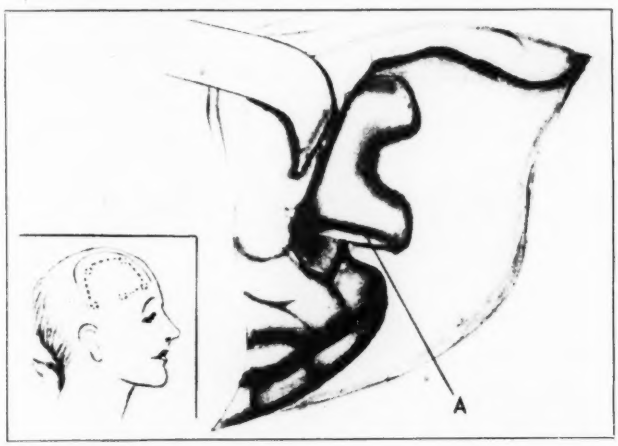

Fig. 2.—Drawing of the optic nerves and chiasm made at the time of operation. *A* indicates incision in the optic nerve.

With these data, the diagnosis of tumor in the region of the optic chiasm was made and operation performed (C. C. C.) on September 13, with avertin anesthesia (90 mg. per kilogram of body weight, supplemented by morphine, ⅛ grain [25 mg.] and scopolamine hydrobromide, 1/300 grain [3.3 mg.]). The following operative notes were made. "A moderate-sized right frontal bone flap was turned down after the cutaneous flap had been peeled away from the pericranium. The

brain was not found to be tight, and after tapping the anterior horn of the right ventricle the brain was soft and fell away from the floor of the anterior fossa. The dura was opened transversely at the middle fossa and the optic chiasm was brought into view. Both optic nerves were seen and both appeared to be three or four times their normal size. This swelling noticed in the optic nerves extended into the chiasm which also seemed many times its normal size and on palpation would fluctuate. It gave the impression of being cystic. A needle puncture revealed the presence of yellow fluid in the chiasm. An incision was then made into the chiasm and extended forward into the right optic nerve; 4 or 5 cc. of yellow fluid escaped. In view of the fact that no great enlargement of the ventricles was demonstrated either by the ventriculogram or the encephalogram, it was thought at the time of operation that the cystic condition of the chiasm and optic nerves accounted for the patient's symptoms. There was no hemorrhage from

Fig. 3.—View of the brain showing the tumor and cystic cavity after medial sagittal section.

the base of the brain, and after good visualization of the chiasm had been obtained the dura was replaced in its former position but not sutured. After hemostasis had been obtained over the dura, the bone flap was replaced and the cutaneous flap sutured with fine black silk. A small rubber tissue drain was inserted beneath the cutaneous flap. The patient stood the operation extremely well and was returned to her room in good condition."

The postoperative diagnosis was glioma with cystic formation of the optic chiasm and nerves.

On the day of operation vision was only perception of light; the next day it was ability to count fingers at 6 feet; three days later, ability to count fingers at 10 feet with easy recognition of colors.

In the following week the patient had an unexplained fever and headache which subsided (probably a cold). Vision became somewhat worse and showed no further improvement. On discharge from the hospital (September 27), the pupils were dilated and sluggish to light; vision was only perception of light. The gen-

eral condition was good. There was no headache or drowsiness, and neurologic examination gave negative results except for the eyes.

The patient subsequently grew steadily worse. Dr. Hileman noted vision practically nil, respiratory embarrassment, headache and vomiting (December 2). He did a lumbar puncture which gave relief of symptoms for nine days; lumbar puncture was repeated with relief again. Vision appeared to be better for a time.

Death occurred on Jan. 9, 1933. Autopsy was performed (limited to the head). The brain was sent to Dr. Percival Bailey of the University of Chicago.

The following, in substance, is the pathologic report submitted by Dr. Bailey.

Gross Examination.—The surface of the brain showed the convolutions to be flattened and the leptomeninx somewhat thickened. On the inferior surface one saw a bulging mass occupying the region between the tips of the temporal lobes and the anterior surface of the pons. The mass seemed to be cystic, and in the center of it one could distinguish the stalk of the hypophysis. The olfactory bulb was visible on the left side. The anterior communicating artery and anterior cerebral arteries were easily recognizable. Just back of the anterior communicating artery one saw the thin wall of a widely dilated third ventricle. The optic nerves and chiasm were greatly thickened. The posterior communicating arteries were easily recognizable on either side of an apparently cystic mass occupying the region of the infundibulum. The optic chiasm seemed to be greatly enlarged and a cystic cavity extended out into the right optic nerve. The cystic mass extended backward, making a depression between the cerebral peduncles and indenting the anterior surface of the pons anterior to and above the posterior cerebral arteries. The mass of the optic chiasm could be traced backward on either side into the optic tracts. The enlargement did not involve the optic tracts. The optic nerves, however, were probably involved and enlarged, but had unfortunately been cut off very close to the enlarged mass of the chiasm.

Left Half, Medial Sagittal Section: The aqueduct of Sylvius was not dilated. There was a cyst which projected upward from the infundibular region and displaced upward the floor of the third ventricle. The lower part of the interior of this cyst was filled with a cheesy, grayish-yellow material. The upper part of the cyst wall was fairly smooth. This cyst extended backward as far as the tegmentum of the midbrain, upward posteriorly to the massa intermedia and anteriorly until it pushed the pillar of the fornix anteriorly and upward. The lateral wall of the cyst separated readily from the left lateral wall of the third ventricle down to about the level of the hypothalamic sulcus. In addition to this, there was another cystic cavity which did not communicate either with the cavity described previously or with the third ventricle. This cavity lay anteriorly and extended from the region of the anterior commissure downward into the chiasm and left optic nerve.

Right Half of the Brain: The wall of the cyst separated from the right lateral wall of the third ventricle, although it was more adherent than on the opposite side. The same two cavities were visible on the right side as on the left, and had no communication with each other.

Therefore, the gross diagnosis was an epitheliomatous tumor of Rathke's pouch with an unusual cystic dilatation of the preoptic recess which did not communicate with the remaining cavity of the third ventricle, but did invade the chiasm and optic nerves.

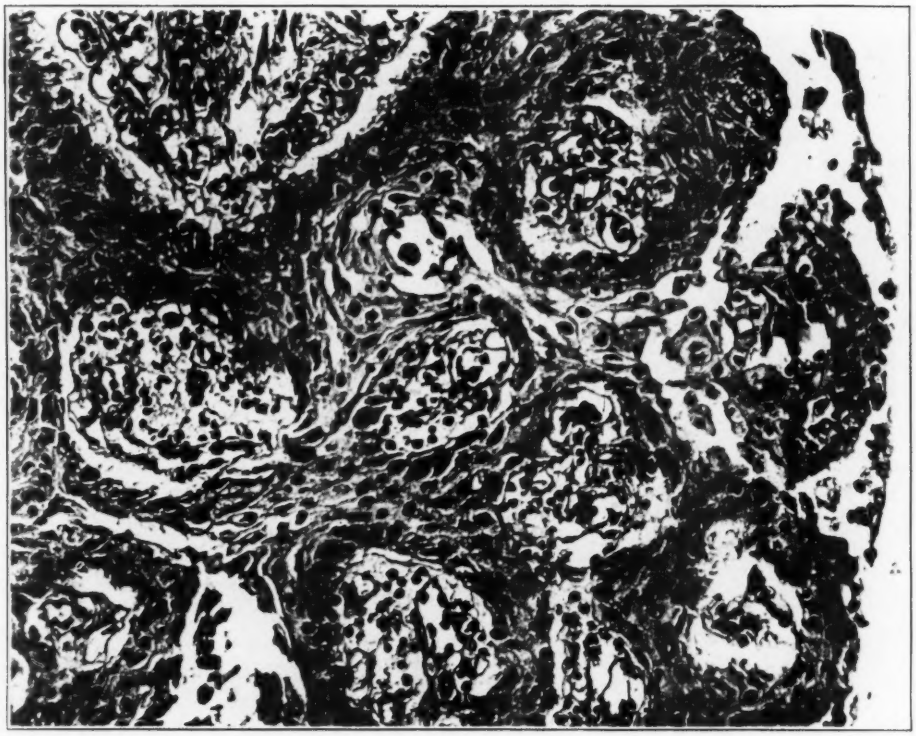

Fig. 4.—Photomicrograph of an epitheliomatous tumor of Rathke's pouch.

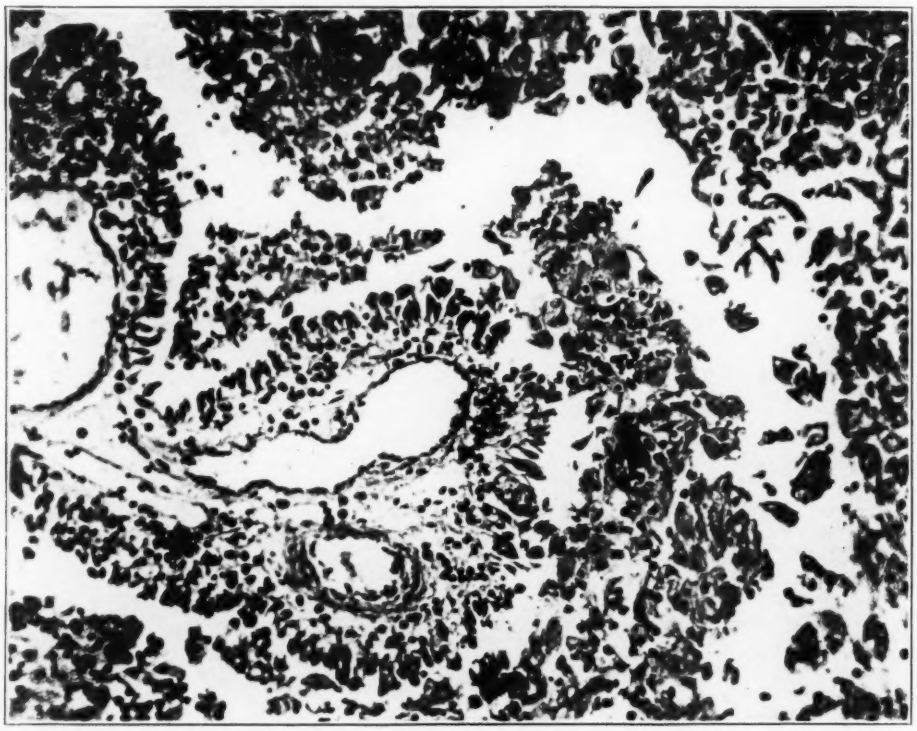

Fig. 5.—Photomicrograph of an epitheliomatous tumor of Rathke's pouch.

Apparently in this case we were dealing with two separate cystic tumors explainable on the assumption of an early embryonic misplacement of tissue belonging to the so-called Rathke's pouch (hypophyseal duct). There would seem to be no doubt that the partly solid, partly cystic, growth behind the chiasm comes in the classification of craniopharyngioma originating from tissue of Rathke's pouch, the proper function of which is to produce part of the hypophysis when separated from the pharynx by the developing sphenoid bone. This tumor had no connection with the cystic growth of the optic nerves and chiasm. The following explanation is offered for the latter: In early embryonic life the fetal cleft is open below. The optic stalks are not yet closed in to become solid cords. Normally the central artery and vein of the retina enter through this cleft to become incorporated inside the optic nerve. Abnormally, interference with the proper closure of the fetal cleft leads to anomalies (colobomas).

Ida Mann [1] said:

> The region of the chiasma can be recognized, as soon as the optic vesicles have grown out of the nerve tube, as that portion of the floor of the fore-brain which lies between the insertions of the optic stalks. It is of course entirely epithelial in structure at first and, when looked at from below, shows merely a smooth convexity lying in front of the region where Rathke's pouch comes in contact with the floor of the forebrain. As development of the central nervous system proceeds, this convex region, which is hollow, projects more and forms a definite ridge uniting the two optic stalks. Their lumina open into its cavity, which can now be called the recessus opticus. The recessus deepens and its wall undergoes differentiation in common with the rest of the wall of the fore-brain, until distinct ependymal, mantle and marginal zones can be recognized at 12 mm. Further cellular differentiation does not occur, since soon after this the marginal layer begins to get filled up with nerve fibers growing into it from the lower surface of the optic stalk.

In view of these facts, may not abnormally placed tissue become incorporated within the nerves and chiasm if it has come in contact with the open optic stalk in early embryonic life? Thus a new growth could develop and a cystic space arise with an ependymal lining as in our case. This accords with the well known theory that tumors are caused by the multiplication of embryonic cells which become displaced during fetal life. In this connection, we may quote Cushing. Speaking of the craniopharyngiomas, he [2] said: "Under this caption are included those lesions which on the Cohnheim basis arise from some cell-inclusion (anlage) in early embryonic life."

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1. Mann, Ida: Development of the Human Eye, New York, The Macmillan Company, 1928.

2. Cushing, Harvey: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1932, p. 93.

It is regrettable that visual fields could not be obtained during the six months' interval previous to this patient's admission to the hospital. Did pressure from behind damage vision and produce characteristic changes in the visual fields, or did the intraneural cyst produce blindness; and what changes in the fields might have been elicited during the progress of this lesion? We can only speculate. The destruction of nerve fibers apparently produced an essential optic atrophy, and presumably the optic sheath was obliterated before intracranial pressure could produce papilledema.

The coexistence of the two independent intracranial lesions in and behind the optic chiasm, both lending support to the Cohnheim theory of the etiology of tumors, is a rare event.

ETIOLOGY OF GLAUCOMA

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Primary glaucoma is a heterogeneous clinical entity, and the present paper deals with only one factor in its etiology—a possible mechanism of a vascular crisis in the eye, such as might result clinically in acute glaucoma. The most dramatic vascular crisis which can be induced experimentally is probably to produce a total cessation of the circulation and then to allow it to start again. This was brought about by raising the intra-ocular pressure to a height above that in the ophthalmic artery by the apparatus seen in figure 1. A cannula (*A*) leading into a glass chamber (*B*), the distal end of which was closed by a membrane (*M*) carrying a mirror, formed an optical manometer recording the variations in the intra-ocular pressure by a beam of light from a source (*L*) on a camera (*C*). The glass chamber was connected by tubing (*D*) to a four-way tube, the other three branches of which connected with a horizontal graduated capillary (*E*), a reservoir containing saline solution (*F*) and a mercury manometer (*G*) with a mercury reservoir (*H*). On the distal end of the capillary (*E*) were a pressure syringe (*K*), accurately controlled by a screw piston, and a small Hürtle manometer (*M'*). The reservoir containing saline solution (*F*) was raised until the anticipated height of the intra-ocular pressure was registered on the manometer (*G*), and, with the saline solution running from the cannula, it was inserted into the eye. Tap *N* was then closed and tap *O* was opened, and the intra-ocular pressure was equilibrated by maintaining an air bubble in the tube (*E*) in a constant position by manipulation of the syringe (*K*). After equilibrium had been established and the pressure noted, tap *P* was shut off and the normal intra-ocular pressure recorded optically. Tap *R* was then closed and the reservoir (*H*) was raised until the manometer registered a pressure of approximately 200 mm. of mercury. With taps *N* and *O* closed, taps *R* and *P* were opened, so that the pressure in the eye was raised to approximately 200 mm. of mercury; that it was maintained at approximately this level was verified by a record from the optical manometer. Tap *P* was then closed, retaining this pressure in the eye and the cannula, and the reservoir (*H*) was lowered until the manometer recorded the normal intra-ocular pressure. After the pressure in the

eye had been maintained at this high level for the required length of time, tap *P* was opened, and the chamber of the eye, communicating again with the manometer (*G*), assumed approximately its original (normal) pressure. This was rapidly equilibrated with the air bubble in the capillary (*E*); tap *P* was then closed, and the subsequent events were observed and recorded optically.

The general blood pressure was recorded in the femoral artery; the state of dilatation of the minute vessels in the iris was observed in the focal beam of a Gullstrand slit lamp; the rate of blood flow was correlated with the temperature in the anterior chamber taken by thermojunctions and registered galvanometrically, and an increase in the permeability of the capillaries was shown by the appearance of trypan

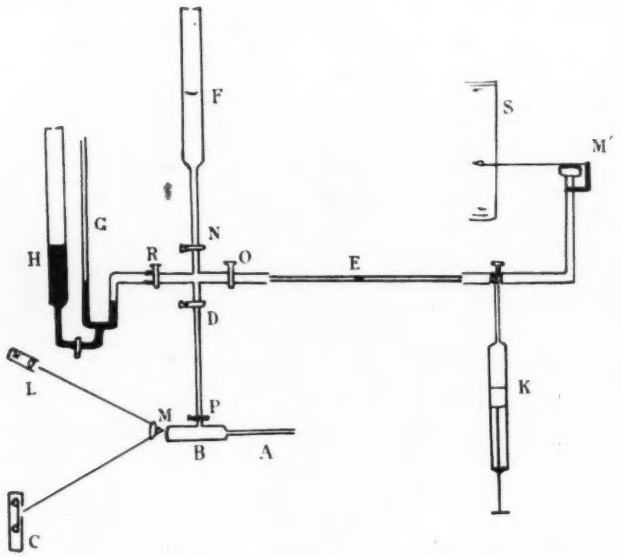

Fig. 1.—The apparatus for raising the intra-ocular pressure.

blue on the surface of the iris and in the anterior chamber after its intravenous injection. In the normal animal the capillaries of the eye are impermeable to this dye; it is detected in the anterior chamber only when the permeability of the minute vessels has been definitely increased, when the presence of a small amount in the anterior chamber is readily visible under the optical conditions employed. In some of the experiments cats were used, under anesthesia obtained with ether and a chloral hydrate and dextrose compound; in other experiments, albino rabbits.

In a series of experiments in which superimposed comparative readings were desired, the optical manometer was eliminated and the cannula put into direct communication with the tube (*E*). The same technic was then carried out, but the intra-ocular pressure was recorded by the Hürtle manometer (*M'*) on the kymograph (*S*). The resultant effects

on the intra-ocular pressure are seen in figure 2. Within thirty seconds after the circulation was allowed to resume, the vessels in the iris were observed to be maximally dilated; the amplitude of the pulse recorded in the tracing became greater; after the intravenous injection of trypan blue the appearance of the dye over the surface of the iris and in the anterior chamber gave evidence of a markedly increased permeability of the capillaries, which after a considerable occlusion was so pronounced that the dye penetrated into the glass chamber of the optical manometer. An increase of blood flow was indicated by a rise of temperature in the anterior chamber of from 1 to 2 C. as measured galvanometrically; the pupil constricted maximally, and after from one to three minutes the intra-ocular pressure rose sharply, as indicated by the optical manome-

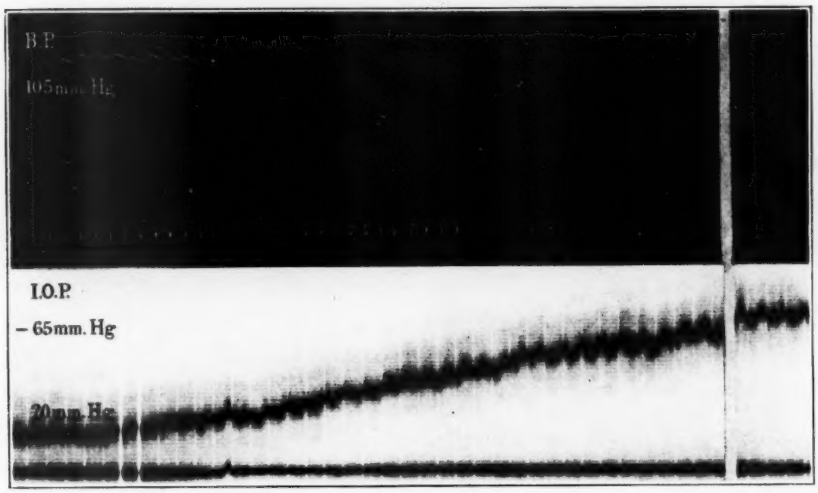

Fig. 2.—The effect of reactive hyperemia after occlusion of the ocular circulation in the cat. The upper curve shows the blood pressure in the femoral artery; the lower curve, the intra-ocular pressure.

ter. The rise of pressure was rapid, and for some time after its establishment the amplitude of the pulse was increased; at a later stage, however, although the increase in pressure was maintained, the amplitude of the pulse declined. In the experiments in which the initial occlusion was maintained for more than sixty seconds (from one to four minutes) the intra-ocular pressure tended to remain high or even to increase indefinitely. These events, especially the maintained maximal dilatation of the small vessels and the constriction of the pupil, seemed to indicate that the cause of the disturbance was the liberation of a histamine-like substance in the eye; and the intravenous injection of the aqueous humor from such an eye into cats showed that a vasodilator substance of this type was indeed present.

These events in the eye at once suggested a close association with the activity of the histamine-like substance which Sir Thomas Lewis [1] and his co-workers have demonstrated to have widespread and potent effects on the skin. It will be remembered that by stroking the skin Lewis produced a reaction which he termed a "triple response." This consisted of (*a*) a local dilatation of the small vessels, (*b*) a local increase in their permeability resulting in the formation of a wheal and (*c*) a widespread vasodilatation which was mediated by a nervous reflex (an axon reflex) and which he termed a flare. This reaction occurs in the skin and conjunctiva; although the first two constituents can be produced elsewhere, as in the liver and spleen, the reflex flare has never been seen in any internal organ. We determined to see if it could be produced in the eye.

A series of experiments was therefore carried out in which the essential feature was to stroke a segment of the iris with the cannula of the manometer as it lay in the anterior chamber.

After the animal had been inoculated intravenously with trypan blue, the cannula of the ocular manometer was inserted into the eye through the limbus (at 3 o'clock) in such a way that its point lay over the iris at the opposite side of the anterior chamber (at 9 o'clock). After the intra-ocular pressure had been equilibrated in the usual manner on the mercury manometer and the optical manometer alone was in communication with the eye, the quadrant of the iris from 7 to 11 o'clock was steadily and firmly stroked with the end of the cannula from six to twelve times. It was possible to do this without any great immediate upset of the equilibrium of the intra-ocular pressure, and the experimental records could always be observed as regular events within one minute after the cessation of stroking. Such a procedure was followed by no appreciable alteration in the general blood pressure except that on several occasions a slight transient fall was observed. In the eye, however, the following changes were consistently produced:

1. Dilatation of the small vessels was noted, after a latent period of about thirty seconds, extending markedly over the area of the iris which had been stroked, and, especially if the stroking had been firm, after a somewhat longer latent period, and to a somewhat less marked extent, over the entire surface of the iris (fig. 3 *B*).

2. An increased permeability of the minute vessels on the surface of the iris was denoted by the appearance of the violet color of trypan blue, at first over the area stroked, and then to a less extent over the entire surface of the iris. It appeared in two or three minutes after stimulation, and after five minutes the entire anterior chamber took on

1. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

a blue tinge; the increase of proteins in the aqueous humor which had escaped from the permeable vessels was at times sufficient to form a clot and block the cannula.

3. A rise of temperature varying from 0.5 to as much as 1.5 C. was recorded on the galvanometer after a latent period of approximately sixty seconds. The temperature then fell slowly and gradually. The duration of the rise was somewhat variable, lasting from ten to fifteen minutes.

4. A maximal and constant constriction of the pupil became evident about thirty seconds after the stroking and persisted indefinitely.

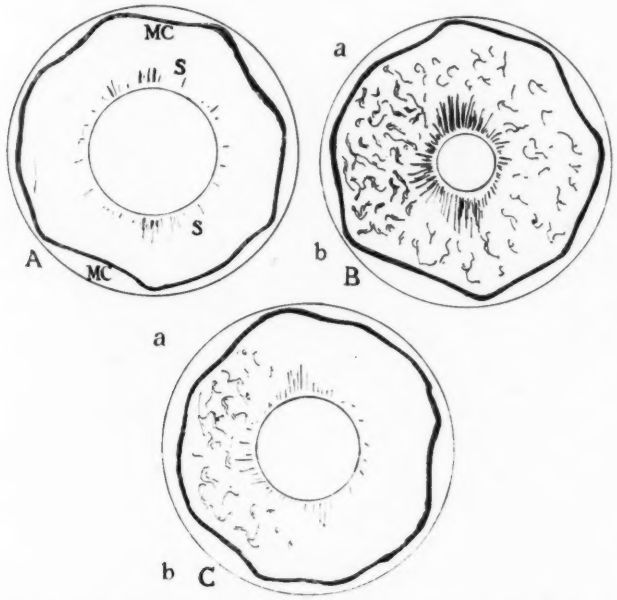

Fig. 3.—*A*, iris of the normal albino rabbit; *MC*, major circle of the iris; *C*, small arterioles around the pupillary margin. *B*, vessels seen in the iris of the albino rabbit after stroking of the segment *a b*. *C*, vessels seen in the iris of the albino rat after stroking of the segment *a b* subsequent to cocainization.

5. A rise in the intra-ocular pressure was recorded starting after a latent period of two or three minutes. The pressure rose slowly and steadily, reaching a maximum of from 17 to 30 mm. of mercury above the normal pressure after from ten to fifteen minutes, after which it tended to fall slightly, never, however, reaching the normal level within the experimental time (fig. 4).

In a further series of experiments we investigated the extent to which this reaction would repeat itself. If the initial stimulation was small, and the resultant response was feeble, as judged by the transudation of dye and the rise in the intra-ocular pressure, a second more

powerful stimulation succeeding the first after from ten to thirty minutes produced a further rise in the intra-ocular pressure and a greater transudation of dye. But if the initial stimulus was considerable, so that the response attained reasonable dimensions, any repetition of the stimulus, while inducing a further vasodilatation of the vessels, was completely ineffective in increasing the transudation of dye and raised the intra-ocular pressure by only a slight amount. This phase of "refractiveness" was found to persist over the longest experimental periods investigated—more than an hour and a half.

A second point of interest which was elicited in experiments subsequent to the occurrence of a well marked reaction was the action of epinephrine injected into the blood stream. Duke-Elder and Colle [2] have already shown that in a normal animal an injection of 0.1 cc. of a

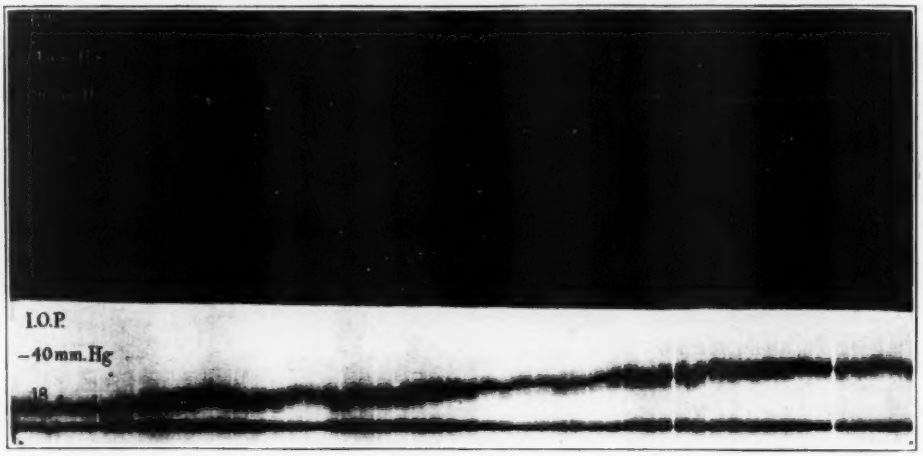

Fig. 4.—Reaction to stroking of the iris in the cat. The upper curve shows the blood pressure in the femoral artery; the lower curve, the intra-ocular pressure.

1 in 1,000 solution of epinephrine hydrochloride produces a local vasoconstriction in the eye sufficient to present a barrier which prohibits the rise of general blood pressure from becoming effective in raising the intra-ocular pressure. In these circumstances, therefore, we obtained a rise in the general arterial pressure, as measured in the contralateral carotid artery, and a fall in the intra-ocular pressure. After a well marked response to stroking had been elicited, however, such a fall in the pressure of the eye could never be obtained, the tracing of the intra-ocular pressure following passively the changes in the general blood pressure (fig. 5).

A similar series of experiments was conducted after a 2 per cent solution of cocaine had been instilled into the conjunctival sac in drops

2. Duke-Elder, W. S., and Colle, I.: J. Physiol. **71**:1, 1931.

at two minute intervals for about half an hour. Such a procedure allows enough of the drug to permeate into the anterior chamber to effect anesthetization. When the stroking was repeated under these conditions a very modified response was obtained. Hyperemia was noted only over the area stroked while the remainder of the iris retained its normal appearance (fig. 3 *C*). The increased permeability of the vessels was also confined to this area, and the blue color was limited to one quadrant of the iris and never tinted the aqueous humor. The pupil was constricted as before, but the rise of intra-ocular pressure was slight in comparison with the previous variation, amounting only

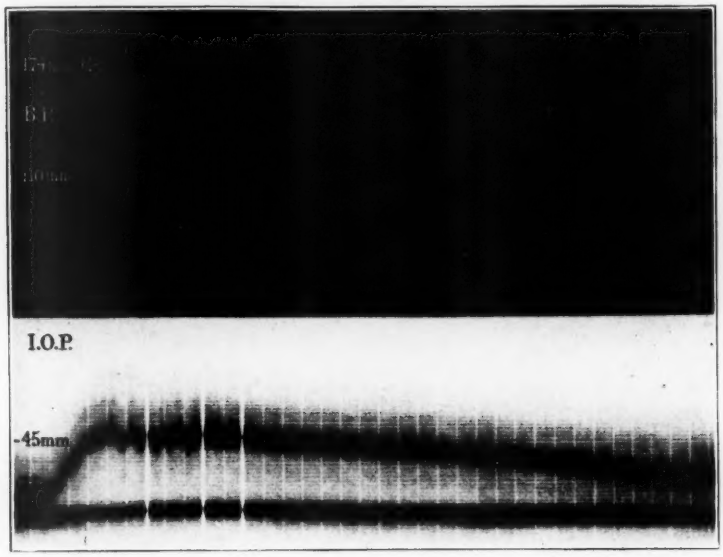

Fig. 5.—The effect of epinephrine hydrochloride (0.1 cc. of a 1 in 1,000 solution) injected intravenously after the reaction to stroking (cat). The upper curve shows the blood pressure in the femoral artery; the lower curve, the intra-ocular pressure.

to 2 to 3 mm. of mercury, and the pressure fell back to approach the normal level in a few minutes (fig. 6).

Apparently, therefore, we are dealing with two types of response, one of which is local in distribution and is independent of nervous activity, and the other of which is general in distribution and takes place only when the nerves are allowed to function. The suggestion at once presents itself that we are dealing with an axon reflex mediated by the trigeminal nerve similar to those described by Bruce,[3] in 1910, in the conjunctiva; and that this axon reflex is a possibility is shown

3. Bruce: Arch. franç. de path. gén. et expér. **63**:424, 1910.

by the effects of sensory stimulation of the cornea. When this tissue is scratched with the point of a needle, the same reaction results, although to a very much smaller degree, as when the iris is injured. The occurrence of this reaction and its absence after the cornea is anesthetized with cocaine demonstrate the participation of the fifth nerve in the response, since branches from this nerve only are found in the cornea.

In will be remembered that Lewis,[1] in 1927, in his work on the reactions as shown by the vessels of the skin, deduced that the triple response was due to the liberation of a substance having the physiologic properties of histamine which was already normally present in the tissues. The occurrence of a slight fall in the arterial blood pressure, the

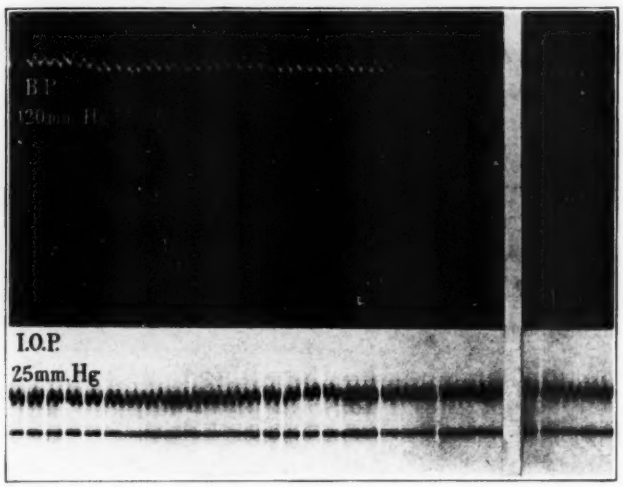

Fig. 6.—The effect of stroking of the iris on the intra-ocular pressure after cocainization (cat). The upper curve shows the blood pressure in the carotid artery; the lower curve, the intra-ocular pressure.

constant development of extreme miosis in every experiment and the close parallelism of the results obtained are suggestive evidence that some histamine-like substance was concerned in the reactions in our experiments. The demonstration of a histamine-like substance in the aqueous seems to complete the case. The most interesting thing about the whole matter is that all previous research—which of course had omitted the eye—had shown that this response occurred in none of the internal organs but was peculiar to superficial structures such as the skin and conjunctiva. It would appear therefore not only that the eye is exceptional in this respect, but that this response is even more easily elicited and more marked than in the skin, a peculiarity which can be explained by the occurrence in the eye of axon reflexes which govern the behavior of its vascular elements. It is well known that the entire

uveal tract is plentifully supplied by a nerve network richly interspersed with ganglion cells, and it is on this basis that the present responses presumably rest. Such a mechanism would certainly explain how a picture of acute glaucoma could arise and why the eye differs from other organs in the violence of its reactions in this respect. It is known that any upset of the metabolism tends to liberate histamine-like bodies in any tissue; and it may well be that the acute vascular crises associated with an increased permeability of the intra-ocular vessels and with the destructive rise of pressure which characterizes acute glaucoma find a possible explanation in the consequences of the liberation of this substance and of the dissemination of its influence over the entire uveal tract by a system of axon reflexes.

These experiments find an added interest because of the work done by Friedenwald [4] some time ago. It will be remembered that from anatomic studies he concluded that acute glaucoma is regularly associated with a vascular lesion localized in the capillaries, and he found that in some cases a transportable vasotoxic substance is present in the intra-ocular fluid. It is evident that there is a mechanism in the eye which can give a very full effect to the action of any such substance.

4. Friedenwald, J. S.: The Pathogenesis of Acute Glaucoma, Arch. Ophth. **3**:560 (May) 1930.

CATARACT AND TETANY FOLLOWING PARATHYROID DISTURBANCE

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There is nothing new in the fact that disturbances of the parathyroids can cause, among other things, opacities in the crystalline lens; this has been established since 1888, when Landsberg reported the first case. Even prior to that cases of cataract associated with tetany or with muscular cramps that were probably tetany were reported. The parathyroids are small and are closely related to the thyroid, so that in operating on the thyroid it is easy to damage them by removal, by interference with their blood supply or by involving them in cicatricial tissue. The outstanding evidence of interference is the development of tetany. Their influence on calcium metabolism shows itself in a reduction of the calcium content of the blood and an increase of phosphorus. About forty-five cases of parathyroid cataract have been recorded, which probably represents a small proportion of the number that have been observed. The two cases that I report seem to conform fairly well to those usually described in respect to history and other characteristics, and the symptoms, apart from ocular symptoms, are well presented in statements written by the patients themselves.

REPORT OF CASES

CASE 1.—Mrs. S., aged 44, was seen in April, 1925. She gave a history of an operation for goiter in 1923, which had been followed by a variable disturbance of vision. When she was nervous the eyes pained and vision became much worse. She saw better in the dark and better with the right eye than with the left. Vision in the right eye was 15/30, and with a minus 0.75 lens, 15/25. The patient was able to read Jaeger's test type number 14. In the left eye vision was 8/200 and with a minus 2 lens was 20/100. The patient was able to read Jaeger's test type number 16. Both eyes showed opacities as large as the undilated pupil in the posterior layer of the cortex of the lens and at the center of the posterior capsule. The opacity was larger and denser in the left eye. The right fundus showed a small round hemorrhage in the retina, ¼ disk diameter in size and 2 disk diameters above the disk. The patient was given a number of injections of lens antigen for the purpose of clearing the opacities, but without effect. Eighteen months after the first examination vision had fallen to 20/200 in each eye with —10.00 and a month later vision in the left eye was for moving objects only.

Extraction with corneal suture was performed on the left eye on Oct. 4, 1926. An attempt was made to grasp the capsule of the lens with the forceps and do an intracapsular operation, but the capsule was so tight, owing to the swollen lens, that the forceps slid over the surface and no hold could be obtained. The lens was

expressed after capsulotomy, and a satisfactory dressing of the wound was made. Five days later the right eye was operated on. The lens was removed in the capsule by the Knapp method. A small amount of vitreous was lost preceding and accompanying the delivery of the lens. A corneal stitch was used, and the tying of this controlled the loss of vitreous. Capsulotomy was necessary on the left eye and was performed one month after the extraction. Three days after capsulotomy the left eye became painful and the tension rose. Physostigmine (eserine) paracentesis and epinephrine failed to control the tension, and after nine days trephination with peripheral iridectomy was performed on the upper temporal quadrant. Eleven days later a hemorrhage was seen on the disk, almost completely covering it. Two weeks later the hemorrhage was seen to have spread toward the temporal side; this was still present one month after trephination, though the tension was 20 and 26. Vision was 15/30+. The hemorrhage had not entirely disappeared in April, 1927, but the condition of the eyes has continued to improve, and in May, 1933, when the patient was last examined, vision was 5/6 and 5/7.5, and she read Jaeger's test type numbers 2 and 1. The left nerve was paler than the right, but was not cupped, and the left field showed an enlarged blind spot and a sector defect below.

The left eye showed an even upward coloboma, with a peripheral buttonhole in the upper temporal quadrant of the iris. In the lower temporal quadrant of the iris was an atrophic patch, below which there was an anterior synechia. Some vitreous could be seen bulging through the pupil. The eyeground was normal except for the pallor of the nerve. The right eye showed the hammock-shaped pupil so often seen after loss of vitreous. Tension was 26 and 24, according to Schiötz' tonometer. Unfortunately, I am unable to report the results of the blood tests made by the internist associated in the case. A description of the symptoms of tetany is given in the patient's own language:

"In compliance with your recent request, I am writing a report of the complications resulting from the thyroidectomy performed on me, on April 19, 1924, by Dr. A.

"The immediate results were disturbance of the parathyroid glands, with severe tetany, which was noticeable in the hands and feet and particularly in the face and the muscles about the eyes, and a spasmodic and twitching sensation which was unrelieved for two years. Bromides were administered during this period by the attending physician, without any helpful results.

"In 1925 I placed myself under the care of Dr. B., who prescribed calcium lactate and 1/10 grain (0.006 Gm.) of parathyroid extract three times daily. This treatment proved inadequate and was supplemented by biweekly doses of parathyroid extract-Collip in doses of 15 minims (0.9 Gm.) taken over a period of one or two years. There was marked improvement in my condition; the tetany of both the hands and feet entirely disappeared. Since that time calcium lactate in doses of one-fourth teaspoonful taken three times daily and a weekly administration of parathyroid extract-Collip have proved sufficient, and, although I am still highly nervous at times, my condition is greatly improved."

CASE 2.—Mrs. B., aged 22, was seen in December, 1923, because of irritation of the eyelids. Vision was 20/20, and she read Jaeger's test type number 1 with each eye. She had had an operation for goiter the previous May. In 1929 she was seen again. In the meantime she had had two more operations for goiter, and her husband had contracted tuberculosis. For six weeks her vision had been failing until she was unable to read, and she had many headaches. The history of her operations and their sequelae are given separately. Her vision was 20/200 in each eye; this improved to 20/25 with glasses, and she read Jaeger's test type

numbers 4 and 3 better with both eyes. Diffuse opacities of the lens, zonular in type, were seen in both eyes; the fundi were normal, and the vitreous was clear. Vision gradually failed, and in March, 1931, it was 4/200 and 5/200, slightly improved by a minus 5 diopter lens. The right lens was needled in March, and a simple linear extraction was done two weeks later. The same operations were carried out on the left eye in June, 1931, and capsulotomy was performed in December. The final result in both eyes was vision of 6/6, with ability to read Jaeger's test type number 1 with round central pupils. The following account of the patient's condition is in her own language:

"In August, 1927, I became ill. I was pregnant, and that had caused a return of my goiter. I had had an operation for goiter in 1923. On Jan. 12, 1928, I was operated on at the Pasadena Hospital, California, after I had been in the hospital about four and a half months during which time my condition was such that an operation could not be performed. In December I was seriously ill for weeks; at one time the physicians said that I could not live through the day. I rallied, however, and my condition improved slowly for a while. But in January, when the blood tests and examinations showed that my condition was becoming worse, the physicians realized that they had to operate immediately. I was given a blood transfusion on January 11 and was operated on the next day.

"I weighed slightly less than 60 pounds (27.2 Kg.) at the time of the operation. Because of my condition the surgeon thought that it would be inadvisable to try to remove all the goiter that should be removed, as he did not know whether I could stand the operation at all, so he operated on one side only, hoping that by doing so he was removing enough to prevent future disturbance. My condition improved immediately and I was able to leave the hospital the latter part of the month. By the middle of February the physicians believed that I was able to travel, and I was brought back to Memphis.

"My condition continued to improve for a while, but in the late spring I began to have trouble with the goiter again. Finally it was decided that the goiter should be removed before the condition developed that I had had the previous winter. On Aug. 6, 1928, Dr. A. operated on me at the Baptist Hospital.

"Tetany began less than a week after the operation. My hands would draw until they formed a cup, my feet would draw as though they were cramping, the muscles about my eyes and face would twitch, and the muscles all over my body would draw and twitch. Dr. A. did not know what was causing the drawing. He gave me thyroid extract in an attempt to stop it and hypodermic injections to relieve the pain. The condition improved slowly, and I was able to sit in a wheel-chair and walk a little with the help of a nurse when I was not having the drawing and twitching. These continued for about a month. Dr. A. was unable to relieve the twitching and drawing and admitted that he did not know what was causing them.

"Finally, on August 13 Dr. A. called in Dr. B. to see if he could make a diagnosis. Dr. B. inspected my chart, examined me thoroughly and then ordered a blood calcium determination. This was carried out the following morning. As soon as Dr. B. received the report he said that my condition was caused by lack of parathyroid. All the muscles in my body were twitching and drawing that day. He gave me a hypodermic injection of parathyroid extract-Collip early that evening. Within an hour I was sitting out in the sun parlor feeling well; there was no trace of twitching. Two days later Dr. B. ordered a second blood calcium determination to decide whether another injection of parathyroid extract-Collip would be necessary. It was not, and I was allowed to leave the hospital that morning.

"As I remember, this injection was all that was necessary for about three weeks, at the end of which I had to have a second one. I do not remember how many injections were necessary between then and the last of October, but the number was not large. When I was taken to the physician for an injection of parathyroid extract-Collip I had to be helped in; I would go in dragging my feet and scarcely able to walk owing to the drawing and twitching. After I was given an injection my pulse was watched carefully; in about fifteen minutes I would have a rigor. After that I would continue to lie down for a few minutes and then would get up feeling well and would be able to walk out of the clinic.

"The worst attack I ever had was in the latter part of October. I had been suffering from the drawing and twitching more or less for several days. Then one night it became worse. My hands cupped and were drawn toward my arms, my feet were drawn, the muscles around my eyes were twitching and caused my eyes to water as though I were crying, and the muscles all over my body were drawing, pulling, it seemed to me, in the opposite way from which they should. This lasted all night; by morning I was nearly screaming from the pain caused by the muscles having been pulled out of place such a long time. Mr. B. got in touch with Dr. B., who prescribed something which he thought would give relief. I took that, but it did not lessen the drawing. Attempts to locate Dr. B. later in the morning were unsuccessful. Finally the nurse at his clinic told Mr. B. that if he would bring the parathyroid extract-Collip she would give me a hypodermic injection in case Dr. B. had not arrived when we got there.

"I was finally taken to the clinic and had to be practically carried in. By that time the drawing was so bad that my arms were bent at the elbows and I could not straighten them out; my hands were cupped and drawn back toward my arms, the muscles about my face and eyes were twitching, the muscles all over my body were drawing so I could not straighten up, and my feet were drawn as though they were cramping, until the toes, instead of being straight, were curved. I was put to bed immediately and given a hypodermic injection of parathyroid extract-Collip. This, however, did not give relief. I was kept at the clinic all afternoon. Several hours after the first injection it was necessary to give a second. The drawing lessened, but this and the twitching continued all that night.

"At the onset of the tetany all my movements would be slow and my nerves would be on edge. I would always be drowsy. The day following a hypodermic injection, I would be sore all over as a result of the drawing of the muscles.

"Following the last attack I had to have one or two injections daily for some time. At first I had to be taken to the clinic for all of them. Later my sister was allowed to give them to me at home after she had given one before Dr. B. so that he could be assured that she could give them properly.

"From that time on I had numerous attacks. Often my jaws would lock so tightly they could not be pried apart. For some time I could not walk because the muscles of my legs and feet drew so badly. If I was moved from the bed I had to be picked up and carried. Practically all the time I could detect the approach of an attack by the way in which the muscles around my eyes would start twitching and the way in which my hands would begin to draw and cup.

"It was necessary for me to have so many hypodermic injections for the tetany that they ceased to cause rigor, and often they did not relieve the drawing for hours, sometimes not until the following day. As the injections seemed to be losing part of their effect, Dr. B. gave me some small phenobarbital tablets to take when I had the drawing so that the injections might be delayed as long as possible and thus might be more effective. He also began to give me parathyroid extract, two tablets to be taken after each meal. He said that they had

never been as effective as the injections. I took them for two years along with the injections, and, while they may have helped, they never seemed to ease the drawing or twitching in any way.

"By the middle of December the attacks were not quite so frequent, and by taking the phenolbarbital tablets, when necessary, I was able to go several days without an injection and was able to get out a little.

"In February I began to have severe headaches. Dr. B. took roentgenograms of my sinuses to discover if that could be causing the headaches, but there was no trouble with the sinuses. The cause of the headaches was not determined. After I knew that I was having trouble with my eyes I was sure that the headaches were caused by eyestrain. However, they were not caused by strain from reading because during the fall I read practically nothing, and for a month after Christmas I was in bed with influenza and had not read anything during that time. I had been ill so long that I had got out of the habit of reading and seemed to have lost interest in it, so all spring I did not read the daily paper. In May I noticed that the letters seemed to blurr and run together after I had read a few lines.

"Mr. B. had to go away in June for his health. I was so disturbed because of this that I did no reading at all in June. One day in July I picked up a paper, only to discover that I was unable to read the print. I could read handwriting if it was in ink, but I would sometimes have to look at it several minutes before I could read it, and then I could read only a few lines at a time; otherwise the letters would blur and seem to run together so that I could not make them out.

"I gradually reached the point where I was having the hypodermic injections further apart. I had had so many of them that they did not always have an effect. Sometimes I would take one and then ten days would elapse before I took another, without any effect on the tetany. Near the end of the summer I could sometimes go as long as a month without an injection, but when I did this I usually had to take quite a number of phenobarbital tablets. There was no regular schedule in regard to the injections. Several weeks might elapse between them, and again it might be necessary to follow an injection with another one two or three days later. During that time I was taking little exercise. When I stirred around much it was necessary for me to take the injections oftener.

"Even after the tetany seemed better and the hypodermic injections were given at longer intervals, I might be sitting down or moving about when a muscle without warning would jerk or twitch. It might be a muscle in my face or in my body or limbs. These movements reminded me of the sudden jerks of frog legs.

"All that winter I continued to have hypodermic injections, when necessary, and to take the parathyroid tablets three times a day and the phenobarbital tablets when needed. In the summer of 1930 I began to take sun baths and daily walks, increasing the length of the walks every day. I began to feel better, and the injections were farther apart; sometimes there was an interval of six or seven weeks between them; but in order to go that long without injections I was taking the phenobarbital tablets like candy, literally eating them. Dr. B. thought that in time it would not be necessary for me to have the hypodermic injections or take any other medicine, and every time I saw him he told me to continue the same medicines.

"During the winter the tetany seemed to be getting worse, and it was necessary to take more injections than I had been taking. Finally in January I went to consult Dr. C. to ask if he could do anything to relieve the tetany. Various tests were made, and I was given a thorough examination.

"Just after Dr. B. had been consulted he had placed me on a diet without pork, veal, beef or lamb or anything seasoned with them. In the spring of 1930 I was

allowed to have lamb occasionally. Dr. C. said that I could eat anything I wanted. He outlined a diet for a normal person, with certain foods to be eaten each day; there was nothing that I could not have. He also gave me tablets of thyroid extract to be taken one a day, as basal metabolic studies showed a slight lack of thyroid. He told me to take nothing else except one bottle of cod liver oil to build up my general health. He believed that the condition was partly a nervous one caused by so much surgical intervention and by fear of further attacks. I soon began to feel much better, and it was three weeks before the drawing returned. Dr. C. told me to take a hypodermic injection of parathyroid extract-Collip and gave me a calcium compound to take.

"While Dr. Ellett was treating my eyes I took numerous hypodermic injections for the drawing, as well as the calcium preparation. I took an injection on August 2. On August 7 I went to see Dr. C. He gave me a prescription for a new kind of calcium preparation, calcium gluconate, which he said was much more effective than anything tried before for this condition. I was to take a teaspoonful after each meal. Since that time I have had to take no hypodermic injections and have had no trace of tetany; at the same time I have been able to get about more than any time since I was taken ill four years ago.

"I was in Dr. C.'s office a few days ago. He told me that it had been learned that calcium gluconate was more effective when taken about thirty minutes before meals, because when it was taken just before or after meals the system did not get the full benefit of it, as part of the calcium usually passed out of the system with the food. He also told me to take a tablet of oscodol after each meal for a while, as it has been discovered that unless one of several different medicines is not taken part of the time along with the calcium the teeth will decay."

COMMENT

Parathyroid cataract has been so recently reviewed that it is not necessary to do more than recall the outstanding peculiarities of the condition and refer to two recent articles, one by O'Brien [1] and one by Weinstein [2] of Bucharest. In both of these articles the literature is reviewed; this is done especially well by O'Brien. In summary of the second case reported in this article it may be said that cataracts in young people, especially in young women, should be examined from the point of view of possible tetany, especially if one or more operations for goiter have been performed. This form of cataract is more frequent in young women because they are more subject to goiter. Tetany may or may not be present, but the calcium content of the blood serum is apt to be increased and the blood phosphorus diminished. Operation is the only procedure which is likely to help cataracts. Before operation parathyroid hormone should be administered and the intake of calcium should be increased. The tendency to spontaneous intra-ocular hemorrhage, referred to by O'Brien, was present in the first case reported in this article.

1. O'Brien, C. S.: Cataract of Postoperative Tetany, Arch. Ophth. **7**:71 (Jan.) 1932.

2. Weinstein, P.: Brit. J. Ophth. **17**:236, 1933.

INTRACAPSULAR EXTRACTION IN HIGHLY MYOPIC EYES

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The extraction of a cataract from a highly myopic eye has until now been fraught with anxiety for many operators. First, there is danger of prolapse of the vitreous body which is caused by the great prominence of the eyeball and by the usual existence of anomalies of the vitreous body. Second, it is well known that the myopic eye reacts acutely to any operative trauma; therefore, the danger of postoperative iridocyclitis, glaucoma and detachment of the retina is much more threatening. In order to clarify the knowledge of these matters, I have made an account of all extractions for cataract in myopic eyes which have been performed by myself and by the younger assistants (by the latter in about 20 per cent of the cases) in my clinic in the last three years, from April 10, 1930, to April 8, 1933. There were 136 cases. In all of the cases, with only a few exceptions, the extractions were performed according to my intracapsular method, which is described in my book, "Intrakapsulare Starextraktionen." [1]

The following points are the most important. The usual general examination and preparation of the patient are carried out; then follow the instillation of homatropine, anesthesia with 3 per cent cocaine, and a retrobulbar injection of 2 cc. of procaine hydrochloride with epinephrine. My bridle suture is made through the superior rectus; then section with a Graefe knife in the limbus upward about 150 degrees (that is, about two fifths of the circumference of the cornea), suture through the conjunctival flap and incision of the root of the iris with the de Wecker scissors are done. My capsule forceps is then introduced into the anterior chamber, catching the capsule below the lower margin of the iris and by slow movements tumbling the lens, while the squint hook presses on the lower margin of the cornea. The suture is closed, the iris is replaced, physostigmine (eserine), 1 per cent, is instilled, the wound is painted with 5 per cent tincture of iodine, and an ointment of 1 : 5,000 mercuric oxycyanide and 1 per cent physostigmine is placed in the conjunctival sac. A bandage is placed on both eyes, a tin plate being used as a protecting shell. A bandage is left on for about six days, but is changed every day.

1. Elschnig, A.: Intrakapsulare Starextraktionen, in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1932.

The only modification of this procedure is as follows: In very prominent eyes and if there has been trembling of the iris and therefore a suggestion of subluxation of the lens, I insert a suture according to the manner of Liégard before making the section.

In many of the 136 eyes the myopia could be diagnosed only after the wound had healed. I have regarded as myopic those eyes which, after healing, required a correcting glass of less than +8 diopters, which would correspond to a glass of at least —5 diopters before extraction. After extraction, there have been many cases requiring from 0 to —10 diopters. In 114 (83.8 per cent) cases extraction was performed without iridectomy (simple extraction); in 85 cases the intracapsular extraction was successful (+), and 11 times the capsule ruptured during the expulsion of the cataract, but was nevertheless extracted (±). Eighteen times the capsule could not be caught or had already ruptured in the anterior chamber (—).

In the cases of simple extraction prolapse of the vitreous occurred 4 times. Among the 18 cases in which the capsule could not be caught, there was 1 expulsive hemorrhage after an uncomplicated extraction. That is the only eye which was lost. There was no instance of prolapse of the iris.

Iridectomy was performed, especially when the operator was a younger physician, in eyes in which the pupil could not be dilated to at least 5 mm. (senile rigidity of the iris or synechia from mild iridocyclitis) with homatropine, if directly after the section a quite liquid vitreous body flowed out (8 cases), or, finally, if the iris could not be sufficiently replaced after the extraction.

Among these combined cases (except those in which the vitreous body flowed out directly after the section), there were prolapses of vitreous body in 8, or 6 per cent, mostly at the hands of the younger operators. This is more than double the percentage which occurred in cases of extraction of simple cataract which my pupils and I performed. In the last 600 intracapsular extractions without iridectomy, vitreous prolapse occurred in 1.1 per cent. In no case was there infection or severe iridocyclitis.

In 19 myopic patients the cataract was extracted from both eyes on the same day. Nine times the same result was obtained in both eyes; 6 times, one eye +, and the other ±; 4 times, one eye +, and the other —. On 8 patients (16 eyes) simple extraction was performed; on 7 (14 eyes), combined extraction; on 4, simple extraction in one eye and combined extraction in the other. In no case was there prolapse of the vitreous body or of the iris.

The results in regard to vision were as follows:

Vision	Times
6/6 to 6/12	45
6/18 to 6/24	37
6/36 — to 6/60	37
Less than 6/60	17

Among the 17 patients with vision of less than 6/60 is the aforementioned one whose eye was lost because of expulsive hemorrhage and 2 who had previously undiagnosed tabetic atrophy. In 1 case detachment of the retina occurred. This patient had diabetes, with 3.2 per cent sugar and frequent acetonuria. Six weeks after operation detachment of the retina developed, perhaps because of a fistula in the wound caused by a few threads of gauze. In all the other cases in which vision is not at least 6/12, the sole cause has been myopic changes of the yellow spot.

In comparison, I should like to mention that ten years ago I charged my assistant Dr. Spitzer to publish the results of extracapsular extractions in highly myopic eyes. There were 258 cases. Of 173 patients on whom extraction was performed without iridectomy, 6.3 per cent had prolapse of the vitreous body and 2.5 per cent prolapse of the iris. Among 49 patients on whom combined extraction was performed, 12.2 per cent had prolapse of the vitreous body; 2, postoperative infection; 2, postoperative glaucoma, and 2, detachment of the retina.

SUMMARY

A comparison shows that in highly myopic eyes intracapsular extraction is much superior to extracapsular extraction in respect to all complications. In comparison with extraction in nonmyopic eyes, the danger of prolapse of the vitreous body is a little greater, but if all the safety procedures that I have introduced into intracapsular extraction are observed, the final result is not worse than that in normal extraction of cataract in emmetropic or hypermetropic eyes.

THE FIRST MEDICAL REFRACTIONISTS

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"Unlike our ophthalmological forebears, we can no longer send our patients to a dealer in spectacles to select a suitable pair." Thus wrote the great historian of ophthalmology in 1892.[1] A hundred years ago there was not a physician in any country who prescribed the glasses his patients should wear.[2] Indeed, it was not physicians, but physicists and physiologists, from Kepler and Descartes to Helmholtz and Donders, who studied the problems of refraction of the eye. A century and a half elapsed following the work of Kepler before a physician, William Porterfield, a fellow of the Royal College of Physicians of Edinburgh, published in 1759 a "Treatise on the Eye, the Manner and Phaenomena of Vision." This work of two volumes dealt comprehensively with the subject, added much useful knowledge and was specially adapted for study by physicians interested in the eye. Half a century later, Thomas Young, who was a physician as well as a great natural scientist, added his lasting contributions to ophthalmic knowledge.

It must not be assumed that the physicians were not at all interested in refraction during this period. Nevertheless, the works that appeared on diseases of the eye devoted only a few lines to definitions and short descriptions of anomalies of refraction, and referred to the use of spectacles. Bartisch, in 1583, wrote a chapter on protecting oneself from the need of glasses, and another, on ridding oneself of the habit of wearing them. De Saint-Yves [3] described the "three sorts" of vision, "the good sight, that of myopes and that of the presbytae," and mentioned the need of spectacles. But, like Bartisch, he too has a chapter on "How to be Exempted from the use of Spectacles." Beer, of Vienna, in the early years of the nineteenth century, in his textbooks and in his booklet on the "Care of the Eyes," inveighed, as did Bartisch 200 years before, against what he termed the rage of wearing

1. Hirschberg, J.: Einführung in die Augenheilkunde, Leipzig, Georg Thieme, 1892, pt. 1, p. 84.

2. Hirschberg, J.: Geschichte der Augenheilkunde, in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, vol. 13, p. 281. (As single exceptions, it is recorded that in the sixteenth century, Hollerius in Paris, then Mercurial in Italy, and Forest in Holland prescribed glasses for myopia.)

3. de Saint-Yves, C.: Nouveau traité des maladies des yeux. The first edition was published in 1722; the English translation was published in London in 1741.

glasses and the harm that they do! Two engravings which adorn the booklet illustrate his feeling on the subject.[4]

The choice of lenses was left to the venders of spectacles, and to the person seeking their aid. In his "Physico-Medical and Chirurgical Treatise on the Human Eye," published in Edinburgh, in 1788, de Gravers stated: "It would now be the proper place to speak of the effect of spectacles on the sight; but as this subject belongs to the optician, I shall not encroach here upon his right." Beer, in 1817, wrote: "The myope must select his own glasses." Opticians also essayed to give advice. Thus, Petit Pierre, optician to the king of Prussia, wrote a "Guide for the Preservation of the Eyes," published in Berlin in 1828.

"Skilled opticians" on their part found fault with the "common spectacle venders." Alexander Alexander, practical optician and optician in ordinary to their Royal Highnesses, the Duchess of Kent and the Princess Victoria, wrote "A Treatise on the Nature of Vision, Formation of the Eye, and the Causes of Imperfect Vision," published in London in 1833, which lists as subscribers such distinguished names as Astley Cooper, Dalrymple, Farre, Tyrrell, Babbage and Travers! He said:

> If the dangers and inconveniences arising from the use of common spectacle glasses, manufactured by wholesale from all sorts of defective materials . . . oft times even from common window glass . . . passed off on the public by the various puffings of the day . . . if these things were seriously reflected on by the public, the experienced and skilled optician would not have occasion to repeat so often to poor creatures who have been led away by such absurdities, and who apply to him for assistance, that it is out of his power to render it, the eye having become actually morbid, by the use of defective glasses.

In the second quarter of the nineteenth century, the interest of the medical profession in errors of refraction grew, and evidences of this interest appear in widely scattered places. In England one finds a long and interesting account on the "Various States of Defective Vision" in the excellent treatise on the eye by Mackenzie[5] of Glasgow (1791-1868). However, he advised that "When a near-sighted person wishes to be fitted with concave glasses, the simplest and surest plan is to try a series of them at an optician's shop."

Nevertheless, there were physicians who had spoken words of caution. Van Maanen,[6] who in 1794 won a prize for his book on the

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4. Hoyer, in a historical retrospect, stated that "50 years ago it was rare to see young persons wearing glasses; they were looked on as dudes" (J. d. Chir. u. Augenh. **24**:615, 1836).

5. Mackenzie, William: A Practical Treatise on Diseases of the Eye. The first edition appeared in London, 1830; the second, in 1835; the third, in 1840, and the fourth, in 1854.

6. van Maanen, cited by Hirschberg,[2] vol. 14, pt. 5-7, p. 106.

use of spectacles, urged that no one buy a pair of spectacles without seeking the advice of a physician. He also condemned the too frequent use of glasses. It is evident that physicians had an undue fear of the harm that glasses might cause, and when they discussed their use, it was to warn rather than to recommend.

The first to utter a new note was Fronmueller, the son of an oculist in Fuerth,[7] himself a physician specially interested in diseases of the eyes. In 1843, he wrote "Ophthalmologische Notizen"[8] criticizing oculists who leave the selection of glasses to opticians, just as though one would permit the apothecary to fix the dose of a medicine! Fronmueller had a trial case made for himself with sixty of the commonly used strengths, and a spectacle frame.[9] "In this way, the proper glasses can be selected for each eye and harmony of vision obtained."[10] Fronmeuller determined the glasses that were to be worn and sent the formula to the optician to be made up! But trial cases alone did not suffice for tests of refractive errors, and it seems a curious coincidence that in the same year in which Fronmueller's paper appeared, Kuechler, a physician in Darmstadt and director of an ophthalmic clinic in that city, published the first test letters. They were arranged for the reading distance, and the purpose was to express changes in visual acuity and differences in vision between the two eyes.[11]

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7. Fuerth appears to have been a great manufacturing place of glasses, 200,000 dozen pairs being made there a year.

8. Fronmueller: J. d. Chir. u. Augenh., 1843, vol. 32.

9. Trial cases had been arranged in earlier times. Rohr (Geschichte des Brillenkastens, Ztschr. f. Ophth.-Optik. **13**:107, 1925) described a case arranged by an optician, Hirn (1719-1799), who worked in Mannheim and later in Munich.

10. Tauber, an optician, tested each eye separately and recorded the near and far point, using a page of a certain German print about the size of Jaeger 11. Holke employed his records of 1,200 cases as the basis of a medical dissertation in 1830.

11. Schriftnummerprobe fuer Gesichtsleidende, in Hirschberg,[2] vol. 14, pt. 2, p. 405. Dr. Kuechler began his studies in the thirties; at first he used printed pictures of various kinds and sizes, but these were unsatisfactory; later he found letters preferable, choosing them rather than arithmetical figures because their number was not so limited. These, also, proved unsatisfactory, and he had a series of words printed of various sizes, accurately measured. It was this that he published in 1843. Kuechler's test charts, however, appear not to have been much used. Some of the older opticians used print or written matter in selecting glasses. Daca de Valdes of Seville, in his book of 1623, used printed matter, but, also, mustard seeds arranged on white paper; the test was to count them. Mustard seeds were probably selected because the New Testament speaks of them as the smallest of all seeds! He advised using their own wares in the case of dealers in pearls, linen, etc., so that the objects should not appear enlarged or coarsened. Those interested in the history of test types are referred to the essay of Pergens (Janus **10**:419, 1905).

In the following year, 1844, Beger [12] of Dresden, in an address on myopia, urged that the wearing of glasses in schools should be permitted only on medical certificate, and that dealers in spectacles should be under medical supervision!

About this time, Arlt of Prague, later of Vienna, constructed a trial case. His story is thus told in his autobiography: [13]

In 1840, I found no collection of trial glasses in either the Prague or the Vienna clinics. In 1843, I journeyed to Vienna for the special purpose of obtaining such a collection from a reliable optician, Ploessl. In order to possess a useful means of determining the acuity of vision and its increase or diminution during a treatment, I arranged printed matter of various sizes according to the height of the letters measured in lines, though I did not consider the distance of the objects from the eye with the necessary care for I generally examined at the ordinary reading distance (10 inches). . . . In 1846, I published the "Pflege der Augen"; its chief value, in my opinion, lies in the appendix on eye-glasses in which I said: "Physicians, especially those who have chosen diseases of the eye for their specialty, will in the future certainly acquire greater knowledge concerning eye-glasses and their use, and not direct everyone who needs glasses to the nearest optician. They will provide themselves with the necessary trial glasses made by responsible opticians, and not only determine the question as to whether glasses are necessary, but, also, determine the strength of glass to be selected, and give directions for the optician just as they give prescriptions for the apothecary." [14]

Merz, in 1845, in Munich, published "Optik besonders fuer Augenaerzte." In this text one reads: [15]

Some physicians have cases of eye-glasses and adjustable frame (*mit beweglichem Gestell*) with the weaker glasses ascending at intervals of five inches, the medium glasses inch by inch, and the stronger glasses with ½ inch intervals; with their help they work out the prescriptions for the optician.

In Germany there must have been a growing demand for trial cases, for in 1848, a pamphlet was published by the Optical Institute of Munich on a new trial case for oculists.[16]

It is stated that Sichel (who came to Paris from Germany) was accustomed, about this time, to devote one day in each week in his clinic to the prescribing of glasses.[17] It is doubtful, however, whether

12. Beger, cited by Hirschberg,[2] vol. 14, pt. 2, p. 301.

13. Arlt, C. F.: Meine Erlebnisse, Wiesbaden, J. F. Bergmann, 1887, p. 39.

14. The rapidity of change which followed is indicated in the third edition of Arlt's book,[13] in which he wrote: "This statement . . . no longer holds good for a part of the medical and lay public. At this time we rarely find a physician who professes to be an oculist who does not possess the necessary optical knowledge, and the trial cases that I suggested as absolutely indispensable."

15. Merz, L.: Optik besonders fuer Augenaerzte, Munich, 1845, p. 83.

16. Ueber Gebrauch eines neuen Brillenbesteckes fuer Augenaerzte, Munich, 1848.

17. Sichel, cited by Hirschberg,[2] vol. 14, pt. 3, p. 97. Sichel had studied in Wuerzburg, then became an assistant of F. Jaeger in Vienna in 1827 and settled in Paris in 1829, where he continued to practice until 1858.

the exercise of this practice by oculists at this time was of much advantage to the patients, for there was still great confusion concerning some very elementary facts. Thus, Sichel, in his book on spectacles, published in 1845, forbade the use of convex glasses for distant vision, even by the aged, and William Cooper, as late as 1853, took off the convex glasses from a child of 8 years with high hyperopia; this in spite of the fact that Janin in 1772 had shown their need, and that Wells in 1811, Ware in 1812, Mackenzie in 1830 and others had published more advanced views.

Contributions were coming fast. In 1854, Edward Jaeger published his small but memorable book on "Staar und Staaroperationen." In this book he explained his purpose in arranging a practical and, at the same time, an accurate, method of measuring vision; his test letters and charts accompanied the volume. He pointed out their many advantages to physicians and to opticians in the selection of spectacles. Jaeger's test charts, less well known, are especially interesting; they consist of two series of vertical lines arranged like the pales in a fence, seen in perspective; they are of accurate measurement and are arranged in logarithmic order.

In practice, however, Jaeger was not yet able to loosen the bonds of century-old traditions. He wrote a preface in 1855 to a booklet by Rospini,[18] an optician, in which he refers to the mad fashion (*Modethorheit*) of wearing glasses, against which he "cannot warn too insistently," just as Beer had done half a century before. Jaeger's "simple, practical method consists in letting the patient try out glasses of different numbers until he finds one with which he can read and write just as well as if he had perfectly healthy eyes." This is the way in which glasses were obtained in Vienna in 1855. In Hasket Derby's "Recollections" [19] one reads that in Vienna in the winter of 1859, "Cases of refraction seemed comparatively rare in those early days. . . . Astigmatism was then unknown, and the choice of glasses by the surgeon rather than by the optician was only beginning to be practiced." In Germany, similar conditions prevailed. Reute,[20] in his "Lehrbuch der Ophthalmologie," published in 1853, still left the selection of glasses to the optician.

In the modern era, the study and treatment of refractive errors became subjects of real concern to the medical profession. In 1855, Stellwag von Carion [21] of Vienna published his "Accomodationsfehler

18. Rospini: Brille und Fernrohr, Vienna, 1855.

19. Derby, Hasket: Personal Recollections of Graefe, Arlt and Donders, Arch. Ophth. **2**:237 (Sept.) 1929.

20. Ruete, C. G. T.: Lehrbuch der Ophthalmologie, ed. 2, Braunschweig, F. Vieweg u. Sohn, 1853.

21. Stellwag von Carion, C.: Accommodationsfehler des Auges, Sitzungsb. d. Wien. Akad. d. Wissensch., April, 1855.

des Auges," in which he distinguished *Weitsichtigkeit* or presbyopia and *Uebersichtigkeit* or hyperopia. He also published a test chart, the first to indicate the distance at which each line should normally be seen!

In the meantime, a star of the first magnitude had appeared—Hermann von Helmholtz. In 1851, he published his epoch-making pamphlet describing the ophthalmoscope. In 1856, his "Handbuch der physiologischen Optik" appeared. This was the turning point. It is interesting to have a contemporary expression of judgment such as that of Herman Knapp,[22] who in an address in 1862, stated:

> It is certain that having been given the means to clearly recognize the deep ocular affections (with the ophthalmoscope), this also led oculists to develop the tests of the functions of the organ of vision in the most extensive and accurate manner. In fact, this chapter has undergone a complete reformation in the last ten years.[23]

Donders, who had published a number of ophthalmologic studies, applied himself to the problems which the ophthalmoscope and the errors of refraction presented. In 1858, he published "Hints on the Use and Selection of Spectacles." [23] He used Jaeger test types 19 and 20 at 7 or 8 meters, and he examined eyes and prescribed glasses. In 1860, Donders had two sets of words printed larger than Jaeger's largest, and in 1862 he printed a new set, this time of letters only. In the same year, he wrote that Snellen was preparing his test charts. His "Astigmatismus und cylindrische Glaeser," [24] appeared in 1862, and was followed two years later by his "Accommodation and Refraction of the Eye." [25] These works produced a revolution in the attitude of the medical profession to the problems of refraction. The work on "Refraction and Accommodation" appeared in 1866 in German and later in other languages and met with universal acceptance. It is one of the ophthalmologic works which deserves to be called classic, in the sense that its value is enduring. In simple and clear language, the age-long confusion between hypermetropia and presbyopia was finally and completely removed.

Cases of astigmatism had been described before Donders' [26] time. Thomas Young had discovered the condition in his own eyes, and had had a cylindric glass ground to correct it in 1793. Gerson, in 1810, showed that the anomaly was due to irregular curvature of the cornea.

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22. Knapp, Herman: Die geschichtliche Entwickelung der Lehre von Sehen, Wiesbaden, C. W. Kreidel, 1862, p. 25.

23. Donders, F. C.: Arch. f. Ophth. **4**:301, 1858.

24. Donders: Astigmatismus und cylindrische Glaeser, Berlin, 1862.

25. Donders: Accommodation and Refraction of the Eye, London, New Sydenham Society, 1864. The work had been written in Dutch, was translated by W. D. Moore and was dedicated by Donders to his friend, William Bowman.

26. Donders,[23] p. 539.

Airy, the astronomer, had again made the discovery in 1827, and his friend Whewell gave the condition its name, "astigmatism." Dr. Isaac Hays of Philadelphia, in his American edition of Lawrence's "Treatise on the Diseases of the Eye," in 1854, added an interesting account of McAllister's success in dealing with cases of this kind, but it remained for Donders to make known how frequent and important these errors are, and how they are to be dealt with. It is of great interest to learn that a French medical officer, Goulier, sent a sealed manuscript in July, 1852, to the Paris Academy in which he cited the frequency of astigmatism and the number of cases in which it had been corrected. The Academy did not publish this paper until 1862, and then only at the urgent advice of Javal.[27]

In the German edition of his book of 1862, Donders told that in his effort to determine the degree of astigmatism in a convenient manner, he sought to have glasses of various strengths easily obtainable, and Schweigger, who was the translator, stated that the Berlin firm of Paetz and Flohr furnished him with a set while he was preparing the translation.[28] In 1864, Donders [29] wrote:

> As the ophthalmoscope is important for the objective diagnosis of defects of the eye, so is a collection of spectacle-glasses for their subjective investigation. Such glasses are indispensable for the determination not only of anomalies of refraction and accommodation, but also of the accuracy of vision, so that without them the examination of the functions of the eye is impossible.

He mentioned the trial case of Paetz and Flohr,[30] calling attention to the differences between the strength of these glasses and to those of Nachet of Paris, because of the difference in the Prussian and the French inch, and recommended Nachet's.

In 1866, Donders [31] wrote:

> The number of communications is constantly increasing, showing that practitioners as well as physiologists are having cylindrical glasses ground and worn with success for the correction of astigmatism.

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27. Mauthner, L.: Vorlesungen ueber die optischen Fehler des Auges, Vienna, W. Braumüller, 1876, p. 876.

28. Donders,[24] at the end of the preface.

29. Donders,[25] p. 139.

30. Donders,[25] p. 97, footnote: "Paetz and Flohr, opticians, unter den Linden, Berlin, supply such boxes with the necessary positive and negative glasses. The boxes contain, moreover, prismatic and colored glasses, with a spectacle-frame. Jaeger's spectacle-frame, prepared by Kraft und Sohn, mechanicians, Vienna, Stadt, Karrnerstrasse, 1043, im Buergerspital, is convenient; the rings containing the glasses are movable, allowing their distance to be regulated so that the patient can look nearly through the center of both glasses."

31. Donders,[25] German edition, Vienna, O. Becker, 1866, p. 456.

As mentioned previously, it was Donders' colleague, Snellen in Leyden, who in 1862 published his work on standard test types.[32] John Green, forty years later, looked back on this as "marking the beginning of systematic testing of acuteness of vision in clinical work.[33]

In France, Sichel had, in 1848, published his "Leçons cliniques sur les lunettes et les états pathologiques consécutifs à leur usages irrational." In this he followed the time-honored views. The new conceptions were brought to France in 1862 by Dorr, who published a French translation of Donders' "Astigmatism and Cylindrical Glasses"; in 1865, Monoyer translated another monograph of Donders on the "Anomalies of Refraction of the Eye and Their Consequences"; in the same year (1865), Giraud-Teulon's book on accommodation and refraction appeared; in 1866, Javal published his translation of Donders' great work "Anomalies of Accommodation and Refraction of the Eye"; in 1867, von Helmholtz's "Physiological Optics" appeared in a French translation by Javal and Klein, and in 1867 a booklet on "Des lunettes et de leur emploi en oculistique" was published by Fano. The influence of von Graefe through several of his pupils who in the early sixties settled in Paris must also be mentioned in this connection. I refer especially to Liebreich, de Wecker and Eduard Meyer; the first two settled in Paris in 1862, the latter in 1863.

I have already referred to the trial cases of Nachet. They are mentioned by Donders (in 1866), who tells that they "have been making them for some time." Through my friend, Dr. Magitot, I obtained the following information (translation) from Mr. A. Nachet, the grandson of the founder and the president of the present company:

Sir:

Here is the information concerning the box of trial lenses for which you asked me which you can tell your friend Dr. Friedenwald. Javal, Donders and Col. Goulier worked over cylindrical lenses, and the latter had even before this time placed a sealed letter in the Paris Academy which was opened on the advice of Dr. Javal. In 1859, Dr. Liebreich,[34] having great difficulty with the lenses with which he was working, asked Mr. C. Nachet for a way of obviating these difficulties. It was in answer to this request that the first boxes of trial lenses were made. I verified this information from the memory of one of my old uncles who in his youth knew Javal, Donders, Col. Goulier, Liebreich, Follin, etc.

A. NACHET.

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32. Snellen, H.: Probebuchstaben zur Bestimmung der Sehschaerfe, Utrecht, P. W. van de Weijer, 1862. The year 1862 was prolific in the introduction of new test types, for not only did Snellen's appear, but, also, Dyer's in America, and that of Giraud-Teulon who took his idea from Donders.

33. Green, John: Tr. Am. Ophth. Soc. **10**:190, 1903.

34. Liebreich was assistant to von Graefe from 1854 to 1862.

It is interesting to add a note of Derby's:

> The trial cases, rudely constructed, contained no cylinders. Even after astigmatism became known, the cases were furnished with but one row of cylindric glasses. The first that contained a double row was made for me by Nachet, under protest. He could not see what I needed it for.[35]

I shall now turn my attention to England. Increased interest of the medical profession is evidenced by the appearance in 1847 of "Vision in Health and Disease; The Value of Glasses for its Restoration and the Mischief caused by their Abuse," published by Smee, F.R.C.S. and surgeon to the Central London Ophthalmological Hospital. In 1854, a second edition appeared. Smee described test types for the reading dstance similar to Jaeger's, and he made a lengthy reference to astigmatism.[36] His book appeared again in 1864, but even then he appears to regard the selection of glasses as the function of the optician, for, after describing his optometer, he said that it "should invariably be employed by the optician before glasses are sold to the applicant."

The first one to bring the newer views to the attention of the English medical profession was J. Soelberg Wells.[37] In 1860, he wrote:

> There are perhaps few subjects connected with ophthalmic practice which demand greater care and exactitude than the choice of a pair of spectacles. The very frequency with which we are called upon to improve vision by means of glasses is but too apt to make us somewhat careless and empirical in our mode of selection, and to prescribe those which the patient himself most fancies, even although they may not quite accord with the range of his accommodation, or with the scientific principles which should influence our choice. . . . I would urgently advise the adoption of a method practised in many parts of the Continent. In Berlin, for instance, von Graefe has spectacle boxes, containing convex and concave glasses (whose number corresponds exactly with those kept by the opticians); from these he selects the proper glasses, and puts the number of their focal distance on a slip of paper, which the patient takes to an optician, who supplies him with the spectacles thereon prescribed.

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35. Derby,[19] p. 255.

36. "For irregular refraction, I find it recorded that the Astronomer Royal devised lenses having a cylindrical curve on the one side and a spherical on the other, which would magnify or diminish more in one direction than the opposite. I have, however, never seen such a lens; and although I wrote to the party who is said to have constructed them, did not obtain an answer to my inquiries. Cylinders magnify in one direction, but not in the other; so that, in regarding print through their agency, the print is distorted into the form of the writing over marine-stores, provided the cylinder be parallel with the lines. If it be placed transversely, then the letters are made to appear ridiculously wide, and separated from each other by great intervals. An ordinary convex lens, placed obliquely, has the same effect." (P. 65.)

37. Wells, quoted by Collins, E. Treacher: The History and Traditions of the Moorfields Eye Hospital, London, H. K. Lewis & Company, 1929, p. 115.

I am fully aware that this proceeding would, at present, be carried out with some difficulty in England, owing to the fact that different opticians often number their glasses differently; but I have no doubt, that if the leading opticians would adopt a certain stand, the others would soon follow their example.[37]

In his "On Long, Short and Weak Sight and their Treatment by the Scientific Use of Spectacles," published in London in 1862, Wells again described the plan, and stated that the "spectacle boxes, which contain a great number of convex and concave glasses, prisms, coloured glasses, etc., may be obtained of Mr. Pillischer, 88 New Bond Street."

A year later, a book on optical defects of the eye was published by J. Z. Laurence. He stated:

I may here call attention to the fact, that, in the French trial lenses, the focal lengths are given in Paris inches, whereas English opticians give theirs in English inches. Twelve English inches equals about 11¼ Paris inches; so that, e.g., if we find a patient requires a 22½ inch glass of the French trial glasses, we should order him a 24 inch English glass. In the German trial lenses (Paetz & Flohr's) the Prussian inch is adopted, which differs but slightly from the English inch.

Whilst these sheets were going through the press, my attention was attracted to a very interesting paper on astigmatism, by Javal (Annales d'oculistique, for January and February, 1865). The following extract contains a new method of determining the existence and amount of astigmatism.

A description of Javal's astigmatic chart follows.

A few years later (1869), Wells published his "Treatise on the Diseases of the Eye," the first English work to deal comprehensively with the newer developments of ophthalmology that followed Helmholtz's invention of the ophthalmoscope, the new system of physiologic optics, Donders' work on refraction and accommodation and the clinical researches of von Graefe and his school. Here one reads:

The affections of the refraction and accommodation of the eye are daily assuming more importance, and are engaging more and more the attention of some of our most able and scientific ophthalmologists. For it is known that certain forms of asthenopia and amblyopia, which had in former times set all remedies at defiance, are not due, as was generally supposed, to serious lesions of the inner tunics of the eyeball, but are in reality dependent upon some anomaly of the refraction of the eye, or a peculiar asymmetry of the organ (astigmatism). Since the discovery of these important facts, a considerable group of cases has been found to be amenable to treatment; cases which had formerly sorely puzzled the oculist, and were by him but too often deemed incurable [p. 255].

I shall now take up the history of the subject in America. In the first half of the nineteenth century, conditions here were like those in England and on the Continent. Here, too, were booklets dealing with spectacles, superficial and popular. Frick's "Treatise on the Diseases of the Eye, including the Doctrine and Practice of the Most Eminent Modern Surgeons and particularly those of Professor Beer," was published in 1823, and Littell's "Manual of the Diseases of the

Eye" published in 1836 presents the eighteenth century views. Littell said:

> Oculists are often consulted about the selection of glasses [referring, of course, only to the quality of the glasses]. . . . If properly selected, glasses afford the greatest aid and comfort . . . without diminishing the sight, though the contrary is vulgarly imagined [p. 255].

William Clay Wallace of New York, a little known American ophthalmologist of that period, was engaged during a number of years in most searching investigations. Between 1835 and 1850, he published studies on the minute anatomic structure of the retina, the ciliary body and related subjects, and two books, "A Treatise on the Eye, Containing the Discoveries of the Cause of Near and Far-Sightedness, and of the Affections of the Retina, with Remarks on the Use of Medicines as Substitutes for Spectacles," in 1836, and "The Accommodation of the Eye to Distance" in 1850. His studies also appear in Silliman's *Journal* in 1835, the *London Medical Gazette* in 1842, and in the *Boston Medical and Surgical Journal* in 1844. Sir David Brewster, at the eighth meeting of the British Association for the Advancement of Science, laid before the meeting a series of preparations of the eye made by Dr. Wallace which, he said, were calculated to establish some important points in the theory of vision.[38] Too little is known about Wallace.

In 1849, a "Treatise on the Nature and Treatment of Morbid Sensibility of the Retina," was published by John H. Dix. It had received the Boylston prize of 1848. He described what is now called asthenopia; after laying stress on "rest" he said:

> If the necessities of the patient really oblige him to work with his eyes beyond their ability, some degree of relief is often attainable by wearing, when applying the eyes, a pair of convex lenses of very low power. . . . When they are resorted to, the patient not being presbyopic, those of any exceedingly small convexity should be chosen. Until recently the least convexity obtainable at opticians was of forty-eight inch focus. Now, lenses may be very generally found of sixty inch focus, and an optician of Paris, at the suggestion of M. Sichel, has manufactured some of ninety-six inch focus; the curvature of these last being hardly distinguishable from a plain surface.

The second half of the century was ushered in with the publication of an English translation of Sichel's book by Henry W. Williams.[39]

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38. Brewster, cited (*a*) by Hubbell, A. A.: Development of Ophthalmology in America, 1800 to 1870, Chicago, A. M. A. Press, 1908, p. 100; (*b*) by Hirschberg,[2] vol. 14, pt. 5, p. 39; (*c*) by Wood, Casey: American Encyclopedia of Ophthalmology, Chicago, Cleveland Press, 1917.

39. Sichel, J.: Spectacles, Their Uses and Abuses in Long and Short Sightedness and Pathological Conditions Resulting from Their Irrational Employment, translated from the French by Henry W. Williams, Boston, Phillips Sampson & Co., 1850.

Williams, after two years at Harvard, spent three years in Europe, and, returning to Harvard, he was graduated in 1849. In this book the errors of refraction are described in the old terms. In 1862, Williams published his "Practical Guide in the Study of the Diseases of the Eye, etc.," and here one still reads: "When possible, anyone desiring glasses should go in person to select them from the establishment of a good optician," and he tells how to secure them when one lives far away. . . But then one reads what is more important: "I have found a full set of glasses of the greatest service in aiding in the adoption of spectacles in difficult cases, as well as in determining nice questions of diagnosis."

It was in Philadelphia that the interesting event occurred which was referred to previously. McAllister, under Hays' guidance, ground cylindric glasses for two patients. Posey claimed that "Hays, therefore, in 1854, may be regarded as the first ophthalmologist in America to prescribe cylindrical lenses to correct astigmatism." [40]

An interesting group of young physicians is next encountered who studied under von Graefe, Donders and Arlt, and returned to America inspired with enthusiasm for the new science: Elkanah Williams of Cincinnati, who was perhaps the first to bring the ophthalmoscope to America, Hasket Derby, Ezra Dyer, Bumstead, Joy Jeffries and my father, Aaron Friedenwald, who spent a year in study in Berlin during 1861 and 1862, and the following year in Prague and Vienna, Paris and London. Ezra Dyer of Philadelphia, in 1862, published a few sheets of test letters, embodying Snellen's theory. But though they appeared a few months earlier than Snellen's, and though they differed somewhat from Snellen's, he gave credit for them to Snellen under whom he had recently studied in Utrecht.[41] Joy Jeffries who studied in Vienna in 1858 to 1859 brought the Jaeger charts to America. When he showed them to Dr. Dix, who had been trained by Jeffries' father, he told him that he (Dix) had for many years used the print of the Boston Directory for this purpose—a publication with type of varied sizes.

The year 1863 brought the new tidings. Bumstead of New York published "A Few Remarks on Astigmatism Illustrated by a Case." [42] He determined the astigmatism by the use of slits, testing each principal meridian separately and found "— 30" at horizontal axis. He said:

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40. Posey, W. C., and Brown, S. H.: The Wills Hospital of Philadelphia, Philadelphia, J. B. Lippincott Company, 1931, p. 51.

41. Dyer, Ezra: J. Am. Ophth. **10**:191, 1862. These test types are also referred to by Williams in his "Ophthalmic Science," published in Boston, in 1866. Dyer received his degree of M.D. in 1859, went to Dublin, Bonn and Vienna, in the fall of 1860 to Berlin, in the spring of 1861 to London and then to Paris and Utrecht, and returned home in November, 1861, and settled in Philadelphia.

42. Bumstead: Am. M. Times **7**:203, 1863.

> Cylindrical glasses cannot at present be made in this country, or at least in New York, . . . but they can readily be obtained of Messrs. Paetz and Flohr of Berlin and of Natchet & fils, Paris. A complete set should be included in the armamentarium of anyone who makes a specialty of eye diseases.

Soon after, in the same year and in the same journal, Hasket Derby [43] of Boston referred to Bumstead's paper and reported four cases of astigmatism. He likewise sent to Paetz and Flohr in Berlin for the glasses.

Dyer read a memorable paper before the American Ophthalmological Society in 1865, entitled "Asthenopia in Connection with Hypermetropia." [44] Only sixteen years had intervened since Dix's "Treatise on Morbid Sensibility of the Retina" had appeared, but a century of progress separated them.

In 1865, Williams, to whom I have already referred, presented his Boylston prize essay entitled "Recent Advancements in Ophthalmological Science," [45] and here one finds the "recent advancements" described in clear terms. This book also included a sheet of test letters which was contributed by John Green. John Green, in 1867, followed this with an article "On the Detection of Astigmatism," [46] and soon after Pray of Brooklyn suggested the use of letters made of parallel lines placed in different meridians, for the detection of astigmatism.[47] One is prepared, therefore, to read in Joy Jeffries' [48] book published in 1871 that:

> The ophthalmic surgeon alone can determine the kind of glasses to be used. . . . It is the duty of all ophthalmic surgeons to render them of service to the communities in which they live, by continually bringing before them the necessity and value of a thorough scientific investigation of the refractive condition of every eye not perfectly normal. . . . An ophthalmic surgeon alone can make a proper and correct examination of the human eye, and decide what glass, and whether any, should be worn by the patient, and the optician's business should be confined entirely to preparing and setting in a proper frame the glass directed by the former; exactly as an apothecary compounds and puts up the medicine prescribed by the physician.

Such advice as Jeffries gave was needed:

> Risley records the fact that even as late as 1870, the refraction work in the (Wills) Hospital was desultory in character, and that it was still the custom to send aphakic cases to McAllister, the optician, to work out a correcting lens for them.[49]

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43. Derby, Hasket: Am. M. Times **7**:277, 1863.

44. Dyer, cited by Hubbell, [38a] p. 176.

45. Williams, H. W.: Recent Advancements in Ophthalmological Science, Boston, Tichnor & Fields, 1866.

46. Green, John: Am. J. M. Sc. **53**:117, 1867; **54**: p. 82.

47. Pray, cited by Hubbell,[38a] p. 190.

48. Jeffries, Joy: The Eye in Health and Disease, Boston, 1871, p. 42.

49. Posey and Brown,[40] p. 238.

There is no need to carry this narrative beyond 1870.

I have shown how slowly the knowledge of errors of refraction advanced, how for centuries there was groping and confusion, ignorance and traditional error. Toward the end of the first half of the nineteenth century physicians began to apply themselves to practical study of the problems, but even before the dawn of Donders' great work, there were physicians who strove to ascertain and measure variations in vision and errors of refraction with trial glasses and test types. These efforts during the forties of the last century were evidences of the new spirit which had entered into medical study and practice from the physical sciences, the spirit of precision. The test case and the test letters were instruments of precision to measure acuity of vision and errors of refraction.

Knowledge of the facts concerning astigmatism was gained in sporadic fashion here and there at long intervals, and then Helmholtz and Donders appeared, and with the brilliancy of searchlights cleared the paths that had been clouded in darkness and error, solved the problems which had been obscure for centuries and made the correction of errors of refraction an important part of ophthalmic practice.

But it would be an error to consider this the whole benefit of the studies of Helmholtz and Donders. The accurate study of errors of refraction has in great measure contributed to the advancement of the knowledge of diseases of the eye; it has led to accuracy in the study of all the functions of vision, and it has had an influence in fields apparently far removed, that influence which the use of methods of scientific precision exerts in cultivating care in and correctness of observation.

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In November, 1932, a report by Pirie,[1] entitled "Seeing with Closed Eyes," was called to our attention by Dr. James Case. Pirie had noted that when roentgen rays were passed directly through the eyes without the interposition of the fluoroscopic screen a sensation of light was produced. He found that when a radiopaque letter was interposed between the tube and the eye, its shadow was seen as such against a background of greenish fluorescence, so that letters and words could be read. The effect was the same whether the eyes were open or closed. On testing a hundred normal observers, he found that all were able to read letters in this way after dark adaptation of from ten to fifteen minutes. He made use of this phenomenon in localizing foreign bodies in the eye. A radiopaque circle with cross-bars was held before the eye; by the patient's location of the foreign body in one of the four quadrants and its movement with movements of the eye, a fairly accurate localization could be made. Since glass fluoresces in the roentgen rays, he suggested that small fragments in the eye should be seen directly by this method, but gave no reports of cases in which the method was used. Pirie found that patients with dense opacities in the anterior segment, such as cataract, could see the letters if the retinas were intact. No reference to previous work was made, and the author evidently made his observations without knowing of such work. On looking into the subject, a recent article by Taft[2] was found. This author had noted a gray-blue mist in the fluoroscopy room which was present with the eyes closed or open. It became more or less luminous with changes in intensity of the current employed. It was seen only when the eyes were dark adapted. It was apparently not due to fluorescence of the lens since the lenses of persons or animals observed during direct exposure to the rays showed no fluorescence. Taft noted that the movement of a lead screen before the light was seen in a

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1. Pirie, A. H.: Canad. M. A. J. **27**:488 (Nov.) 1932.
2. Taft, R. B.: Am. J. Roentgenol. **28**:245 (Aug.) 1932.

converse direction; that is, the screen appeared to move up as it was moved down. Taft reported the previous observation of the phenomenon by Dorn in 1898 and Röntgen's confirmation of his findings and mentioned some similar experiments made by Edison. In a discussion of his paper, Failla stated that a similar effect is produced by the gamma rays of radium, and Desjardins mentioned previous reports by London and an investigation by von Graefe. This evidently referred to a report by Greef of Berlin, which will be discussed later.

Two reasons why this subject should be of interest to ophthalmologists at once suggest themselves. There is, first, the possibility that the phenomenon might be of practical use in the prognosis for patients with opaque media, especially with senile cataract. Secondly, the fact that the roentgen and radium rays produce a sensation on the retina demands either an explanation through what is known of biophysics and the physiology of vision, or else a revision of these ideas.

In the literature a number of reports dealing with the phenomenon were found dating from the early days of roentgenology.

In 1897, Röntgen [3] stated that G. Brandes was the first to report on the phenomenon, but that he had himself made personal notes on it in 1895, having seen the luminosity of a Hittorf tube through a wooden door. With other tubes no light was visible, but with the later hard tubes it could always be seen. He noted that a slit in a radiopaque substance was seen as straight, curved or circular, according to its position before the eye. He believed that the phenomenon was due to fluorescence produced in the retina. He knew of no evidence that the roentgen rays were refracted by the ocular media or by lenses, as is ordinary light.

At about the same time, the phenomenon was noted by Thomas A. Edison.[4] In 1896, his experiments and similar ones made a short time later by G. Waverley Clark of San Francisco were discussed in an editorial. Edison had reported that blindfolded persons could see objects before the roentgen tube. He had tested a child said to be totally blind who was able to see the hand and other objects before the tube.

In 1898, Dorn [5] referred to work done in 1896 by himself and Brandes. They saw the shadow of such objects as a metal rod against the luminous background of roentgen rays, and noted that the rod appeared curved instead of straight. Dorn found that atropine had no effect on this sensation, so that it was not due to the effects of accommodation; nor did insulation from electric currents which might

3. Röntgen, W. C.: Sitzungsb. d. k. Akad. d. Wissensch. **1**:576, 1897.
4. Edison, Thomas A.: Electrical Engineer **22**:601, 1896.
5. Dorn: Arch. Roentg. Ray **2**:69, 1898.

have produced direct electric stimuli on the retina have an effect. He found that the luminosity was visible to patients with aphacia, so that it was not due to fluorescence of the lens. The observation of Giesel [6] that uranium salts produced a visible phosphorescence may also be mentioned here.

In 1901, Crzellitzer [7] made careful observations on the phenomenon. The tube was focused on the side of the eye and cut off from it by a lead plate with a slit. By moving the plate, various portions of the eye could be exposed. As it was moved backward, no sensation was observed until the slit was back of the location of the lens. This excluded fluorescence of the lens as its origin and indicated that the retina itself must be stimulated. No fluorescence of the cornea or the lens was observed. When the whole posterior segment was exposed, a ring of brighter luminosity was seen, and the sensation was brighter when the region just behind the ora serrata was exposed. An apparent reversal was noted in the movements of opaque bodies before the tube. A hole in the lead plate of 9 mm. appeared to be 1 cm. in diameter, while a lead disk of the same size appeared three or four times as large. Crzellitzer suggested that the method might be of advantage in testing the vision of patients with cataract. In a later article he described the difference between the visibility of the roentgen and radium rays, the former alone being intense enough to stimulate definite areas on the retina. He emphasized the increase in size of the images seen in this way, an object of 4.4 microns being visible.

In 1902, Javal and Curie [8] described the visibility of radium rays and tested patients with ocular disease by this means. Two patients who were totally blind from glaucoma and optic atrophy were unable to see the rays. A patient with retinal detachment saw them in an area of attached retina, while one with dense corneal opacities but some perception of light saw them plainly. London [9] made similar observations with radium. Patients who were blind from optic atrophy could not see the light, and this was true of all patients with no perception of light. Patients with partial optic atrophy saw the light better with the better eye. Patients with cataract saw the light as well as, or even better than, normal persons. He believed that the phenomenon was due to fluorescence of the retina. In spite of this, he apparently believed that the visual cortex could be directly stimulated and claimed that when an area of the occiput was exposed directly, the light was

6. Giesel: Am. d. Phys. u. Chem. **69**:91, 1899.

7. Crzellitzer, A.: Fortschr. a. d. Geb. d. Roentgenstrahlen **5**:245, 1901; Berl. klin. Wchnschr. **40**:650, 1903.

8. Javal and Curie: Wien. med. Wchnschr. **52**:2055, 1902.

9. London, E. S.: Deutsche med. Wchnschr. **30**:784, 1904; Arch. f. Ophth. **57**:242, 1904.

seen. London stated that patients who were partially blind could see letters on a screen exposed to direct radium rays, when they were unable to see them by ordinary illumination. He utilized the method in teaching partially blind persons in schools for the blind.

London's reports attracted much publicity, and the subject was investigated by Greeff [10] at the request of the German government. He concluded that the effect was due to the fluorescence of various objects produced by radium. He stated that opaque objects before the tube were not seen and that the roentgen rays were seen only under special conditions. He believed that London's method depended merely on the fluorescence of the objects themselves and had no advantages over the use of ordinary light. In referring to the work of Himstedt and Nagel, Greeff concluded that the radium rays have no direct effect on the visual cells. His observations and those of certain other observers who were unable to observe the phenomenon indicate that technical difficulties with the machines of the day or failure to obtain dark adaptation was probably responsible. Holzknecht and Schwarz,[11] for example, criticized London's report and denied that radium could stimulate the retina.

The most complete investigation of the phenomenon, from a scientific point of view, is that of the physiologists Himstedt and Nagel in 1901.[12] They noted that when the cornea, lens, vitreous and retina were exposed to radium rays they fluoresced. They found that the visibility of radium and roentgen rays differed in certain respects. The former produced only a diffuse luminosity which was difficult to localize. Solid objects could not be seen by its means, nor could the shape of openings in a lead plate be made out. They found that ultraviolet rays behaved in the same way, producing a luminosity which was cut off by the interposition of a glass plate. They believed that the sensation produced by ultraviolet and radium rays could be explained by fluorescence of the ocular media. With roentgen rays, however, the sensation of light could be accurately localized, and radiopaque objects could be accurately seen by this means. The media of animal's eyes did not fluoresce visibly except for a barely perceptible fluorescence of the retina. This was the same whether the eye was removed in a light or dark adapted state, and hence did not depend on the presence of visual purple. When the rays were thrown on the eye through a hole 4.5 mm. in diameter in a lead plate, the sensation varied with the part of the eye stimulated. If directed at the temporal limbus, as shown by *I*

10. Greeff: Berl. klin. Wchnschr. **41**:452, 1904.

11. Holzknecht, G., and Schwarz, G.: München. med. Wchnschr. **50**:1189, 1903.

12. Himstedt and Nagel: Ann. d. Phys. u. Chem. **4**:537, 1901.

in figure 1, one light spot was seen. If thrown in the direction of *II*, two spots were seen, as the retina was stimulated in two places. The brighter spot was seen at the temporal side. If directed as shown by *III*, at the posterior pole, a line was seen. A slit in the lead screen directed near the posterior pole was seen as a light line, which was almost interrupted near the center in an area corresponding to the macula. Other observations showed that the periphery of the retina is most sensitive to the rays and the macula practically blind to them; hence the sensation must depend primarily on stimulation of the rods.

Himstedt and Nagel repeated the experiments of Fuchs and Kreidl and of Gatti, who attempted to produce optograms on the frog's retina by exposure to roentgen rays after dark adaptation. With ordinary light the visual purple is bleached where it is exposed to light, but

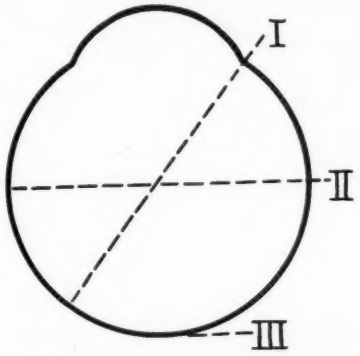

Fig. 1.—Diagram illustrating the experiments of Himstedt and Nagel.

with roentgen rays all observers reported negative results, even after exposure for one hour. Attempts to produce an action current by exposure to roentgen rays, however, were successful. The poles of a circuit, including a galvanometer, were placed at the anterior and posterior poles of the eye, and the apparatus was insulated against induction currents from the roentgen apparatus. When roentgen rays were passed through the eye, an active current developed similar to that produced by ordinary light. An eye exposed to light till it was refractory and showed no further current was refractory to roentgen rays as well as to radium rays (of which only a weak preparation was employed).

Himstedt and Nagel concluded that fluorescence of the retina cannot be excluded as the cause of the sensation produced, but they evidently were not satisfied with this explanation. In other ways the phenomenon behaves like a direct stimulus to the sensory cells of the retina.

From about 1902 until Taft's paper in 1932 little or nothing seems to have been written concerning the visibility of the roentgen and radium rays. We were interested in the phenomenon itself and in its

applicability as a more accurate means of determining the retinal function than the usual tests for projection of light.

It was found that after dark adaptation of from five to six minutes ordinary normal observers were easily able to read the smallest lead letters when these were placed on the roentgenoscopic table without the fluoroscopic screen. The difficulty of finding the letters, which must be exactly in front of the eye examined, made some sort of tube carrying the letters advisable. To meet the case of illiterates, a series of lines and simple figures varying from 5 to 0.2 mm. was cut in a lead slide.

Fig. 2.—*A*, roentgenogram of a lead plate with a visual scale. *B*, the viewing tube with the plate in position; *C*, the viewing tube in use.

This was placed in the tube and fitted with notches so that the size of the object being observed could be ascertained by the examiner in the dark (fig. 2).

Most normal observers could see all the figures on the slide, but some failed to see the last hole, seeing only no. 7, a hole 0.25 mm. in diameter. Since even with the small amount of active radiation employed, usually 5 ma., it was necessary to eliminate all possibility of damage to the crystalline lens, the readings were made quickly; with some slow observers this probably prevented the observation of the smallest figures.

With patients with cataract there was no fear of prolonging the observation. Patients with uncomplicated mature senile cataract saw

figure 5 or 6. Some patients, however, who were old and whose cooperation was not good, failed to see the largest figure, seeing only the light, though their projection of light was good. This seemed to be due to their not understanding what was to be seen or their failure to describe what was seen, since this difficulty was also met with in a few persons with normal eyes. This failure to see the largest figure did not seem to be due to incomplete dark adaptation, as it was present after periods of fifteen or twenty minutes in the dark. The occurrence of this difficulty is, of course, a serious disadvantage, since it may be met with in the very patient in whom knowledge of the retinal function is especially important. Such a case was seen in M. F., who had a mature cataract on the right and severe postoperative cyclitis on the left. He could see only the largest letters with either eye, and though they were seen more clearly with the right eye, the difference was not great enough to justify any conclusions. Another patient, Mr. K., with high myopia and nuclear cataracts, could see only figure 2. His cooperation was not good, however, and it did not seem wise to conclude definitely the amount of myopic degeneration present.

The results were interesting, however, in other patients who cooperated well. In the case of Mrs. K., whose cornea was completely opaque from tuberculous sclerokeratitis, it was supposed that grave danger to the deeper structures had been done. Vision was perception of light with correct projection. Before the roentgen tube, she saw figure 6, while with the left or normal eye only figure 7 was seen. If the question of keratoplasty should come up in such a case, this information would be extremely important.

Mrs. S. had a mature senile cataract on the right with good projection and old iridocyclitis, perception of light and poor projection on the left. Before the tube she saw letters 6 by 5 mm. with the right eye, while with the left only the shadows of larger radiopaque objects could be seen but no letter could be made out.

A girl, Mary B., with congenital glaucoma, had no perception of light with the right eye and perception of light but poor projection with the left eye. With the right eye the light of the tube was not seen, while with the left the light but no letters was seen. Our findings agreed with London's in that patients with no perception of light, whether blind from lesions in the globe or in the optic nerve, perceived no sensation of light from the tube. It must be assumed that Edison's blind patient and several other patients mentioned in the literature really possessed some perception of light. London's belief that the visual cells in the cortex or the nerve fibers of the optic pathways could be stimulated directly was apparently erroneous, as no sensation could be perceived with currents as high as 35 ma. when the occipital cortex was

exposed. As was to be expected, the retina itself must be exposed and must be functionally capable of perceiving light.

Pirie's statement that the fluorescence of glass could be perceived in an eye exposed to the roentgen rays suggested practical possibilities. It was found, however, that while fragments of crown or window glass as small as 1 by 1 by 0.1 mm. when exposed on the screen were seen easily by their fluorescence in a current of from 25 to 50 ma., they were not visible, nor were much larger pieces of glass, when placed in an enucleated rabbit's eye. Nothing else could be expected when it is remembered that the fluorescence consists in the transformation of invisible into visible rays which behave no differently from other visible rays. It is conceivable that a fragment in the anterior chamber would first reveal its presence by such fluorescence, but the reflection of ordinary light from the slit lamp should be almost as effective under these circumstances.

It would seem possible at first thought that by the use of a scale of figures such as was previously described the visual acuity of patients with cataract might be estimated as it would be after operation. It might be thought, for instance, that one who could see a 0.2 mm. object before the roentgen tube could expect an equal acuity after operation. The matter is more complicated than this, however. It must be remembered that the roentgen rays undergo no appreciable refraction by the ocular media. Hence objects before the tube are projected on the retina in their full size.[13] An object of 1 cm. held close to the eye will stimulate approximately 1 sq. cm. of retina. An object of this size is seen as filling a great part of the visual field. Taking the *minimum visible* of the normal eye as an object subtending an angle of 60 seconds of arc, the image of such an object when refracted by the emmetropic eye is estimated to cover 4.2 microns of retina. The smallest object on our scale, about the smallest that can be used in this way, of about 0.2 mm., if its image were not subject to refraction, would cover 200 microns or fifty times that which should be required for visibility. Thus the visual acuity of one who could see such an image should be only about one fiftieth of normal. But, in point of fact, such an object is barely visible to the normal eye before the tube, and is not seen by some normal eyes. This may be explained by the difference between the stimulus of light and of roentgen rays, however their effect is produced. The amount of the latter required to produce maximum visibility of a certain object is not known. We were deterred from using

13. The image is really even larger than the given object, since the rays reaching the object from the roentgen tube are divergent and continue to diverge till they reach the retina. The difference in size would depend on the distance between the retina and the object.

the highest possible currents by the danger of roentgen lesions and used only from 5 to 10 ma. in most of these observations. Aside from these facts, Himstedt and Nagel apparently proved that the visibility of roentgen rays is almost if not entirely a function of the rods, and that the macula is practically blind to their stimuli. Hence in our estimation of retinal function by this means the macular region is practically excluded. In spite of this, in our series of patients, there was a fairly definite relation between the size of the objects perceived and what could be learned of retinal function by other means, but it will require a larger series of cases observed before and after operation to determine how nearly this test of the dark-adapted retina will correspond with visual function.

There remains the most interesting, if quite impracticable, question of how the phenomenon is effected. Do the roentgen and radium rays stimulate the visual elements, or only, as Röntgen believed, produce fluorescence in the ocular media? Himstedt and Nagel, as previously stated, found fluorescence in the vitreous, lens and cornea to be produced by radium but not by roentgen rays. They thought that the retina of an animal's eyes fluoresced slightly in the roentgen rays. Others, as Taft, have seen no fluorescence in the media of patients or in the excised eyes of animals. We can confirm this observation; in addition, we made extracts of the rabbit's retina in saline and in bile, which is a solvent for the visual purple, without determining any fluorescence. This determination was made difficult by the fact that every possible container showed fluorescence when high voltage radiation (from 25 to 37 ma.) was employed. This was true of a quartz tube, a wax container and cellophane. When a concentrated extract was poured on several layers of filter paper, however, no fluorescence was seen, nor did the retina, when removed from the eye, fluoresce visibly. The question of a fluorescence visible only through the visual elements of the eye stimulated which are in immediate contact with the luminous substance cannot, of course, be excluded, but we were unable to obtain evidence of it.

It is generally accepted that the limit of visible light is a wavelength of about 4,000 angstroms, and that the ultraviolet rays of shorter wavelength are invisible. Adler [14] stated that fluorescence in the ocular media may make some of these shorter rays visible. P. Knapp,[15] however, found that patients with aphacia saw the spectrum of the iron arc down to 3,350 angstroms, and concluded that absorption by the lens accounts for the invisibility of the spectrum between 3,350 and 4,050

14. Adler, F. H.: Clinical Physiology of the Eye, New York, The Macmillan Company, 1933, p. 128.

15. Knapp, P., and Bächtiger, P.: Klin. Monatsbl. f. Augenh. **89**:456, 1932.

angstroms which was found for normal eyes. Himstedt and Nagel found that ultraviolet rays produced a sensation similar to that of the roentgen rays and also electrical action currents such as were produced by ordinary light. As stated before, the roentgen rays also produced such action currents. They do not, however, according to these observers, bleach the visible purple in the eyes of dark-adapted animals. In a few attempts we were unable to demonstrate such bleaching.

The roentgen rays measure from 136 to 1.4 angstroms, and the gamma rays of radium from 1.4 to 0.06 angstroms. When high voltage rays are being employed, gamma rays are delivered by roentgenographic apparatus, and in a few very powerful machines the intensity of gamma radiation may approach or equal that of radium.

That such rays produce biochemical changes in living protoplasm is well known, but these changes have been considered to be of an entirely different nature from those produced by visible light. We must conceive of vision, however, as originating in photochemical changes set up in the rods and cones.

It has been assumed that the photosensitive substance present in the visual cells is sensitive only to rays in the so-called visible spectrum. The findings of Himstedt and Nagel and of Knapp, however, show that rays of shorter wavelength may produce a visual sensation when not absorbed by the ocular media. A large part of the ultraviolet rays is absorbed by the cornea and lens, so much, in fact, that it is difficult to produce an abiotic reaction on the retina in eyes in which the crystalline lens is present. It is possible that the amount which is transmitted by the media is insufficient to produce a photochemical effect. Roentgen rays pass the media rapidly, and, on the whole, it seems likely that they do produce a photochemical effect, at least on the rods. The fact that the longer roentgen rays produce a much more definite visual sensation than those of radium would be expected on the basis of this hypothesis. Their failure to bleach the retinal purple seems to indicate a different effect from that by light rays, but it is possible that currents of high amperage may be shown to have a similar effect on visual purple.

CONCLUSIONS

1. The roentgen and radium rays are visible to the dark-adapted eye.

2. There is a difference in their visibility in that the roentgen rays may be localized accurately and that small radiopaque objects may be recognized in their light. The radium rays produce only a vague luminous sensation which cannot be correctly localized.

3. Examination of the vision by means of roentgen rays gives some information as to the function of the peripheral retina in patients with

opaque media. It does not, however, serve in judging of the macular function, and in certain patients the results are unreliable.

4. Care must be taken to avoid injury to the eyes, especially if the lenses are clear, and not more than from 10 to 15 ma. of current should be employed for not more than three minutes. In patients with cataract this amount may be exceeded.

5. It seems probable that the sensation produced by roentgen rays is due to a direct photochemical effect on the rods.

RUPTURE OF THE SPHINCTERAL PORTION OF THE IRIS PRODUCED BY BLUNT TRAUMA

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Blunt trauma of the eyeball, either through the intervening lid or direct, not infrequently produces a rather characteristic tear of the iris. The tear may involve the pupillary portion of the iris or the peripheral portion, or both, but it is my purpose in this paper to speak only of those tears that are confined to the sphincteral portion. This condition is of fairly common occurrence, but as the majority of cases are not reported or are not diagnosed, the frequency of incidence cannot be estimated. Nearly one hundred years ago, Josenhans [1] first described such tears, and since then the literature has been replete with cases. Some of the reports deal only with tears of the pupillary margin of the iris; others with complicating tears of the periphery of the iris (iridodialysis), while in others an associated dislocation of the lens played a rôle.

MECHANISM OF PRODUCTION

Ruptures of the sphincteral portion of the iris are due to blunt trauma of a moderate degree. The exact amount of force necessary to produce this condition cannot be estimated, for so many variable factors enter into consideration that mathematical accuracy is impossible. A certain amount of force is necessary to produce the damage to the tissue, but if that force exceeds a given amount, further complicating damages appear and change the clinical picture entirely. For instance, a light blow of a fist or a tennis ball traveling at not too high a speed can produce a simple rupture, whereas the same factor with but slightly greater force can cause untold intra-ocular damage. The traumatic force, no matter what it may be, can strike the eye direct or may be transmitted through the closed eyelids with identically the same result. Usually, the damaging force is not sufficient to cause more than slight superficial abrasions of the skin or corneal epithelium, and consequently the inflammatory reaction of the external portion of the eye is slight.

The mechanism of the production of rupture of the iris is not fully known as yet. The first explanation was offered by Berlin [2] in 1873, but his suggestions were merely theoretical and have not withstood the

1. Josenhans: Württemb. Correspondenzbl., 1838, no. 41, vol. 6.

2. Berlin: Zur sogenannten Commotio retinae, Klin. Monatsbl. f. Augenh. **11**:42, 1873.

test of time. Arlt,[3] in 1875, made the first practical suggestion as to rupture of the iris when he attributed vast importance to the dilatation of the corneoscleral ring. His contention was that when the eye suffered a blunt trauma, that portion of the envelop represented by the junction of the cornea and the sclera suffered a sudden dilatation outward through the increased pressure of the aqueous and through the compression of the corneal fibers at the point of impact. This theory aroused enormous discussion and is still regarded by many as the true explanation of the rupture. But other factors enter into consideration. In 1869, Caillet[4] proved experimentally that on blunt trauma to the cornea there followed an immediate contraction of the pupil, which later enlarged and formed the well known posttraumatic dilatation. The contraction of the pupil on blunt trauma is probably a manifestation of the so-called orbicularis phenomenon or lid closure reaction. When the endeavor is made to close the lids forcibly, there occurs a simultaneous contraction of the pupil associated with a tendency of the eye to rotate upward. The pupillary contraction is unilateral (not consensual), occurs rapidly and relaxes rapidly, and is known as the Westphal-Piltz reaction. It is supposed to be due to an associated movement of the sphincter pupillae with the facial nerve and probably represents the innervation of association fibers between the third nucleus and the facial nucleus (Behr[5]). This pupillary contraction was evidently entirely overlooked by Collins and Mayou[6] from whose textbook is quoted verbatim:

> The tendency of a blow from a blunt object on the front of the eye is to flatten out the cornea, which has a greater curvature than that of the sclerotic and projects from its surface. Flattening out the cornea forces the aqueous humor backward and laterally. Backward displacement of the aqueous presses on the iris and lens and its lateral displacement widens out the angle of the anterior chamber. The receding iris finds more support centrally from the lens than peripherally from the suspensory ligament. The strain produced by such an injury is therefore felt chiefly at the periphery of the iris, the angle of the anterior chamber and the suspensory ligament of the lens. . . . *The sudden dilatation of the pupil which occurs in concussion injuries* from the displacement backward of the periphery of the iris may cause rupture of the sphincter muscle.

The last statement is unsupported by any proof and is entirely at variance with the experimental work of Caillet. Förster,[7] in 1887, intro-

3. Arlt: Ueber die Verletzungen des Auges, Vienna, Wilhelm Braunmüller, 1875.

4. Caillet: Des ruptures isolées, Thèse de Strasbourg, 1869.

5. Behr: Die Lehre von den Pupillenbewegungen, Berlin, Julius Springer, 1924, p. 36.

6. Collins, E. T., and Mayou, M. S.: Pathology and Bacteriology of the Eye, ed. 2, Philadelphia, P. Blakiston's Sons & Co., 1925.

7. Förster: Ueber die traumatische Luxation der Linse in die vordere Kammer, Ber. über die 19 Versamml. d. ophth. Gesellsch., Klin. Monatsbl. f. Augenh., suppl., 1887, p. 143.

duced into the controversy the view that at the moment of impact the aqueous was driven forcibly backward, carrying with it the iris and lens. About eight years later, Müller [8] elaborated on Förster's idea in stating that, in addition to the increased pressure of the aqueous, the traumatic contraction of the pupil played a rôle in the rupture of the iris. Wagenmann [9] disagreed with this and ascribed the rupture of the iris to the following mechanical movements; dilatation of the corneoscleral ring, the action of the displaced aqueous and the effect of the increased pressure of the aqueous.

From these and other experimental evidences, it would seem that at the moment of impact the following factors play a rôle: (1) flattening of the cornea, (2) compression of the aqueous, (3) displacement of the aqueous posteriorly and laterally, (4) dilatation of the corneoscleral ring and (5) marked contraction of the sphincter iridis. These are all purely results of mechanical pressure, with the exception of the last-mentioned effect, into which there probably enters the nervous reflex arc that lies within the tissue of the iris (Arnold,[10] Münch,[10] Lauber [10] and Pollack [10]). Thus, three factors act simultaneously on the sphincteral portion of the iris, namely: (*a*) the pull of the sphincter toward the center of the pupillary area or the inward force, (*b*) the pull on the tissues of the iris outward by the pull of the corneoscleral ring or the outward force and (*c*) the backward push of the aqueous that is under higher pressure than the supporting lens or vitreous or the backward force. These three forces act simultaneously and momentarily, and the end-result of such action is tempered entirely by the relative value of the three forces. In consequence, the four following clinical conditions may occur:

1. The outward force may be greater than the inward force. If the peripheral pull on the tissue of the iris by the dilatation of the corneoscleral ring is greater than the inward pull by the contraction of the sphincter, the pupillary margin of the iris will rupture at a site opposite to the point of impact.

2. The inward force may be greater than the outward force. If the inward pull on the tissue of the iris by the contraction of the sphincter is greater than the outward pull due to the dilatation of the corneoscleral ring, the periphery of the iris will tear loose at the weakest point and there will result an iridodialysis, usually near the point of impact.

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8. Müller, L.: Ueber Ruptur der Corneoscleralkapsel durch stumpfe Verletzung, Vienna, Franz Deuticke, 1895.

9. Wagenmann, in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, Wilhelm Engelmann, 1910, vol. 9, p. 381.

10. Quoted by Behr: Die Neurologie des Auges, Munich, J. F. Bergmann, 1927, suppl., pt. 1, p. 167.

3. The backward force may be greater than the inward and outward forces. If the inward pull on the tissue of the iris by the sphincter and the outward pull by the dilatation of the corneoscleral ring are fairly well balanced, the backward pressure of the aqueous will predominate and tear the zonule fibers loose at the weakest point, with the resultant complete or partial dislocation of the lens.

4. Any combination of these three results may occur according to the distribution and power of the forces involved, the resistant strength of the tissues and the extent of the site of impact.

As previously mentioned, the first of these consequences is the only one discussed in this paper. At the moment of impact of some blunt object, say, a tennis ball, the corneoscleral ring is forcibly more or less dilated, depending on the force with which this object strikes the eye. At the same moment the reflex traumatic contraction of the pupil occurs. (Moment is used here in a rather broad sense, for undoubtedly several hundredths of a second elapse before the contraction of the sphincter sets in, although this contraction must of necessity occur with a shorter latent period than in a normal light reflex. In a normal light reflex there is a latent period of 0.1875 second. [Gradle.[11]]) But the pupillary contraction is unquestionably weaker than the dilatation force involved. In further proof of this may be stated the fact that the majority of these ruptures occur in brown-eyed persons, in whom the sphincter of the iris is weaker than in blue-eyed persons. Thus there exists a combination of forces which would tend to result merely in a dilatation of the pupil did not a third force intervene. This third force is the increased pressure of the aqueous which at the moment of impact is greatest at the site of impact and least at the opposite side of the chamber from the site of impact. This force travels rapidly and violently across the chamber, driving the opposing pupillary border of the iris before it and acting on that pupillary border somewhat like a sharp, pointed wedge. This wedge-shaped force plus the greater pull of the corneoscleral ring than of the sphincter of the iris results in the separation of the tissues and produces the clinical picture of rupture of the sphincteral portion of the iris. This explanation is purely theoretical, but it combines most adequately the known factors with the known clinical result.

CLINICAL PICTURE

The clinical picture of the rupture of the sphincteral portion of the iris varies greatly. In the majority of cases, an immediate hemorrhage into the anterior chamber occurs. The extent of this hemorrhage depends on the extent of the rupture, which will be discussed later. If

11. Gradle, H. S., and Eisendrath, E. B.: Reaktionzeit der normalen Pupille, Klin. Monatsbl. f. Augenh. **71**:31 (Sept.) 1923.

the sphincter muscle itself is torn, the hemorrhage is apt to be somewhat more extensive owing to the richer supply of capillaries in the sphincter than in the anterior stroma or the posterior pigmented epithelium (Wolfrum [12]). The hemorrhage is seldom extensive enough to fill the anterior chamber with blood, for by the time the torn capillaries have bled enough to cause a 3 or 4 mm. hyphemia, the pressure within the aqueous is equal to or greater than the pressure within the capillaries. Vessels of greater caliber than the capillaries are seldom involved in a simple rupture of the sphincteral portion of the iris, for in this area vessels of such size invariably run a radial course and hence are not apt to be torn by the rupture of the tissue. If the anterior chamber is filled with blood, it is a fair indication that the iris was torn across near the root and that some of the larger radial vessels were ruptured. Again, the amount of bleeding into the anterior chamber may be only microscopic, as was shown in the case of a 16 year old girl who was struck in the eye with a tennis ball, with a resultant rupture of the anterior stroma of the iris and a portion of the sphincter muscle. To the naked eye, the aqueous seemed clear, but in the focal beam of the slit lamp, there could be seen albumin in the aqueous and a large number of freely floating red cells. The latter disappeared within three days. It is not probable that a rupture of the iris could occur without at least some slight hemorrhage into the anterior chamber, and I have never seen a recent case in which red blood cells could not be detected microscopically. The blood, whether microscopic or macroscopic, is prone to disappear within three days after the injury, provided a complicating iritis does not occur.

Immediately after injury, the tear of the tissue of the iris can be seen, if the chamber is sufficiently clear, as it usually is. The tear is completed by the injury and does not enlarge subsequently; neither does it decrease materially in size. The various forces previously mentioned, together with the character of the tissue of the iris and the relative position of the eye at the moment of impact, determine the extent of the tear and the portions of the iris involved. There are three main types of tears of the sphincteral portion of the iris:

TYPES OF TEARS

A. A tear involving the anterior superficial stroma of the iris and but little of the sphincter muscle.

B. A tear involving the sphincter muscle and the posterior pigmented epithelium, with but little involvement of the anterior stroma of the iris.

12. Wolfrum: Mikroskopische Anatomie der Regenbogenhaut, in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, W. Engelmann, 1926, p. 116.

C. A tear involving the anterior stroma, sphincter muscle and posterior pigment epithelium.

A. In point of frequency, these tears range below those of types B and C in the ratio of approximately C 5 to B 3 to A 1. The trauma producing this type of tear is apt to be so slight that the recipient does not seek ophthalmic aid, and the tear is found only incidentally at subsequent examination. The appearance varies slightly in early and in later stages. At first, the delicate meshwork of the anterior stroma around the site of the rupture is apt to be somewhat swollen and discolored, particularly in blue irides. At the site of the rupture itself, the fibrils of the stroma can be seen to be torn and retracted, and to show short loose ends. The appearance is much like that of a finely woven basket that has been forcibly perforated. In the more or less triangular aperture that remains, the surface of the sphincter muscle appears as a flattened brown mass, extending from within a half millimeter of the pupillary

Fig. 1.—Permanent distortion following a type A rupture.

border to well up beyond the apex of the tear. The pupillary border of the iris at the site of the tear is apt to be intact, possibly with a slight retraction of the normally ectropionized pigmented epithelium. If the muscle is torn, some of the posterior pigmented layer can be seen through the hole. On transillumination of the iris, little if any difference between this area and the surrounding normal area can be detected. Shortly after the trauma, the pupil is most apt to be dilated. The ultimate shape and reaction of the pupil depend on the extent of the destruction of the pigmented pupillary margin of the iris and on the extent of the injury to the sphincter muscle. In the type A rupture, the pupil most frequently becomes normal eventually, both in shape and in reaction. However, a permanent distortion may remain as is shown in figure 1. In the later stages of a type A rupture the swelling of the surrounding tissue of the iris subsides and gives place to a low degree of atrophy so that the edges of the rupture are slightly depressed below the level of the surrounding iris. In blue irides, there is not apt to be any change in color, but in brown irides, the edges of the rupture may

become depigmented so that the whole area of the rupture will appear as a brown wedge, outlined by an irregularly white broad band. This is the condition shown in figure 2. The floor of the rupture and the pupillary margin of the iris undergo no further change with advancing time. The damage to the pupillary reaction depends entirely on the extent of the damage to the sphincter muscle and the extent of the repair of such damage.

B. This type of rupture is more apt to follow slightly greater trauma than is found in type A and usually occurs in the thicker irides in which the anterior stroma is composed of more and heavier fibrillae. The lighter colored irides seem to fall into this class to a greater extent than do the deeper brown irides. In this form of rupture, there is invariably a perceptible hemorrhage into the anterior chamber, although the hyphemia may not be sufficient in extent to protrude above the pupillary margin. Owing to the nearly intact anterior surface of the iris, the

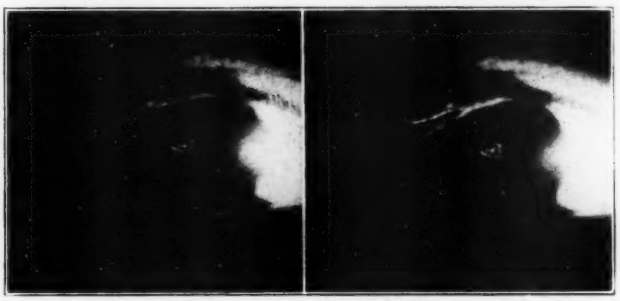


Fig. 2.—Wedged-shaped defect following type A rupture.

rupture is easily overlooked unless searched for, and even then examination with magnification in the focal beam of the slit lamp may be necessary to locate the tear. The anterior surface of the iris has usually undergone no change, although rupture of individual fibers of the iris can be seen in some cases. The posterior fibers of the anterior stroma may or may not be torn according to the extent of the rupture and the amount of force involved. In the early stages, there is at times a slight cloudiness of these posterior fibers owing to hemorrhage within the tissue from the torn capillaries of the sphincter. Through the stroma can be seen the rupture of the sphincter of the iris in the form of a triangular defect of the muscle layer that may extend less than half way through the flat muscle or may involve the entire width of the muscle. The edges of the defect show a definite retraction of the muscle and a tendency toward curling backward. The muscular defect has a parallel defect in the posterior pigmented epithelium, involving the pigmented pupillary border. The defect of the border is, of course, greater than the defect at the apex of the rupture, but without magnification the defect of the

border is more or less hidden by the intact anterior stroma. The extent of defect in the pigment and in the muscle can be seen most clearly on transillumination, in sharp contradistinction to type A. The pupil is more involved than in the preceding type, and the extent of the pupillary dilatation depends on the extent of the rupture of the muscle. In this type, there is apt to be some slight effort at repair, so that eventually the irregular dilated pupil regains some of the lost motion. Unfortunately, this type is difficult to photograph and consequently cannot be illustrated. The extent to which such a rupture is frequently overlooked is illustrated in the case of a young woman physician who consulted me because of a supposed Argyll Robertson pupil. She was on the verge of having a spinal puncture performed, but hesitated, I suppose, for fear of the results of the serologic examination of the fluid. When I informed her that her pupillary irregularity was due to an old type B rupture of the iris which could finally be traced anamnestically to an injury from a tennis ball her relief was unbounded. A little neurologic knowledge is dangerous to the peace of mind.

C. This is the most common type of rupture, and is the only one that occurs at more than one site. In this type, the anterior stroma, the sphincter muscle and the posterior pigmented epithelium are all ruptured simultaneously, so that a more or less triangular defect of the entire structure of the iris exists with consequent distortion of the pupil and more or less immobility of the pupil. It is always accompanied by hemorrhage into the anterior chamber, to a greater extent than in the other two types. Undoubtedly there is greater force involved in the production of the rupture. In this type, the anterior stromal fibers are ruptured cleanly, and straggling ends are seldom to be seen. Even in the dark irides with an excess of chromatophores in the stroma, discoloration of the iris around the rupture occurs infrequently. The muscle and the posterior pigmented epithelium are torn clean through exactly as in type B, and present the same picture when seen biomicroscopically. Owing to the fact that there are no anterior stromal fibers that tend to maintain the rotundity of the pupil as in type B, the pupil in type C is not so irregular, but is more dilated and immobile. The interruption of the pigmented border is more noticeable, and on transillumination the defect blends with the illuminated pupil and does not stand out in such sharp contrast. If more than one rupture is present, there is apt to be one major rupture and from one to four minor ruptures on either side of the major one. Figure 3 shows one large rupture and three smaller ones, all of type C. Here, as in the preceding type, there seems to be a slight effort at repair, although in the majority of cases the defect persists unchanged throughout life. To illustrate again the importance of observing such defects carefully, a large insurance company recently asked me whether my examination of a certain person

about five years ago had revealed signs of tabes other than the irregular rigid pupil of the left eye. Fortunately, my records showed that the pupillary irregularity was due to a type C rupture of the iris and not to a neurologic condition.

PROGNOSIS AND COMPLICATIONS

In any one of the three types of uncomplicated rupture of the sphincteral portion of the iris, there may persist any or all of the following aftermaths: (1) irregularity of the pupil, (2) immobility of the pupil and (3) weakness of accommodation.

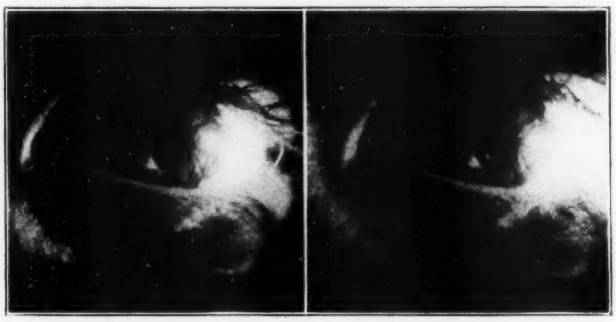


Fig. 3.—One large and three smaller type C ruptures.

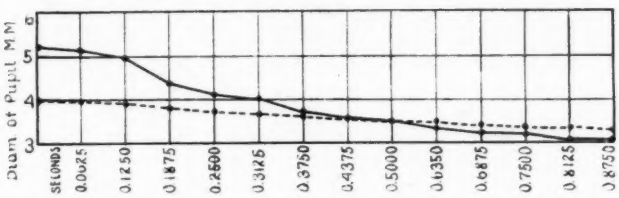


Fig. 4.—Contraction time of a type C rupture, eight months after injury.

The first of these has been discussed under the description of each type of rupture, and it is sufficient to add here that the final shape and size of the pupil depend on the type of rupture and on the extent of damage to the sphincter muscle.

The unruptured portions of the sphincter regain strength and tonicity in the months subsequent to the trauma, so that eventually there is pupillary play in all but the ruptured area. Figure 4 represents the graph of the contraction time of a type C rupture, eight months after injury. The solid line is the graph of the contraction time of the pupil of the uninjured normal fellow eye, photographed cinematographically by the technic described by Ackerman and myself.[13] The vertical ordi-

13. Gradle, H. S., and Ackerman, Walter: Reaction Time of the Normal Pupil, J. A. M. A. **99**:1334 (Oct. 15) 1932.

nates represent the diameter of the pupil in millimeters and the horizontal abscissas, the elapsed time in ten thousandths of a second. The dotted line represents the graph of the contraction time of the pupil of the injured eye and from this can be seen the slowness of contraction and the failure to contract equally and simultaneously with the fellow pupil. This condition will persist throughout life.

There is one other complication that occurs in some cases of rupture of the iris, especially in types B and C, namely, weakness of accommodation. Whether this is due to an actual involvement of the ciliary body or whether it is due to failure of pupillary contraction with its influence on accommodation, cannot be said. But it does occur and may persist for many months, or even for life, regardless of the final outcome of the rupture. In one instance in a girl, 16 years of age, with a type B rupture, accommodation was so reduced that + 1.50 sph. in addition to her correction was required to enable her to read Jaeger's type 1. At the end of two years, this weakness was reduced to about one-half and at the end of four years, no accommodative failure could be detected. In another case with a single type C rupture, a similar weakness of accommodation was found after injury, and this persisted for the six years that the patient was under observation. On the other hand, the eyes shown in figure 3 showed no accommodative weakness, although there were multiple type C ruptures present. So it is impossible to forecast whether or not accommodation will be affected, and if so, whether such a defect will be permanent or not.

There is no treatment of any value in traumatic rupture of the sphincteral portion of the iris.

A fairly complete bibliography can be found in Wagenmann[9] and in Schieck-Brückner: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 4.

EXTRACTION OF CATARACTS

PROF. EMILE DE GRÓSZ, M.D.
BUDAPEST, HUNGARY

In the First Ophthalmologic Clinic of the University of Budapest, of which I am director, 14,000 operations for senile cataract have been performed in the last thirty years, 10,000 of which were done by me. Taking into consideration my previous experience gained while serving as instructor and assistant professor in the same clinic the approximate number of senile cataracts that I have met with amounts to 20,000. Even this number is inconsiderable when compared to the great number of similar operations performed by the ophthalmologists of India, especially by Henry Smith. On the other hand, conditions prevailing in India do not favor thorough observation of each patient and often make the following up of later results impossible, whereas precise records were kept for each patient operated on in my clinic. Except for some cases observed during three years when I acted as head of ophthalmologic departments in community hospitals, the observations reported here were all made in the same institution. Since 1904, when I took the responsibility of directorship, I have performed 65 per cent of all the operations for cataract. At the beginning, I operated on a higher proportion of patients, whereas in later years I made a point of passing on a larger number of operations to my assistants, one of my principal tasks being to provide adequate training for the physicians of my country. I take special pleasure in our achievements in this field, and today there are many skilful ophthalmologists who had their training in this clinic under my guidance.

I have tried various methods of operation for cataract, but I have been careful when changing any of the methods employed, since, in my opinion, there is no value in mere experimentation when one risks failure to achieve favorable results obtained by well established methods. The method employed in my clinic today is the result of several improvements which were found to be useful.

INSTRUMENTS

I shall enumerate a few instruments which are used in my operations:

1. An eye speculum (fig. *A*), which is held by an experienced assistant. It has the great advantage of being quickly removable, if necessary.

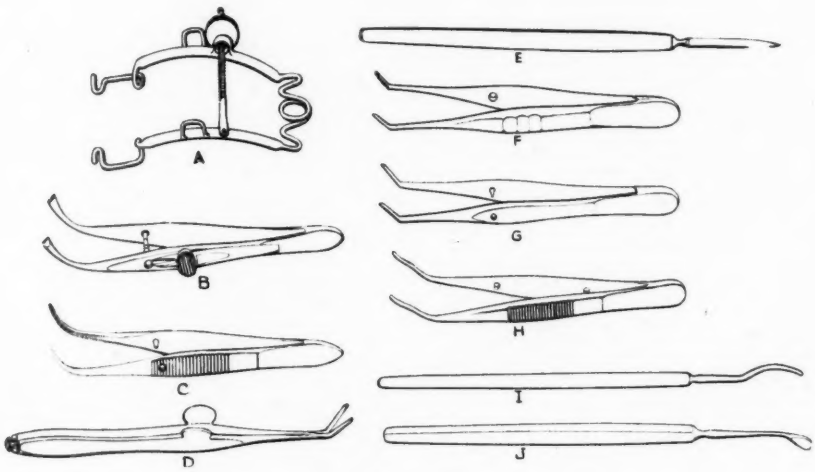
2. A fixation forceps (fig. *B*), which can be passed on to an assistant during iridectomy. Being curved, it is not in the way.

3. Liebreich's iris forceps (fig. *C*) for catching the sphincter of the iris. This instrument is equally adaptable to grasping the iris horizontally on a wide surface.

4. DeWecker's pince-ciseaux (fig. *D*), used in excising the iris by obtaining a cleancut edge and avoiding bruises.

5. Graefe's knife (fig. *E*). The blade is 30 mm. long and 2.5 mm. wide. It can be used in from twenty to thirty operations and its cutting edge remains in perfect condition.

6. Schulek's capsule forceps (figs. *F* and *G*), which serves for the rupture of the capsule. The teeth of this instrument can be polished and thus it may be adapted to intracapsular extraction.



Instruments used in operation for cataract.

7. Elschnig's capsule forceps (fig. *H*), which serves the same purpose as Schulek's forceps.

8. Daviel's spoon (fig. *I*), which is used in delivering the lens.

9. Schulek's expulsor, which is used in delivering the lens.

10. A spatula, which is used in rare instances, in replacing the iris, for the grasping of the iris sphincter. Combined with the pressure exerted by the *pince-ciseax* it produces a coloboma with free pillars.

11. Graefe's spoon (fig. *J*), which is used only when luxation of the lens occurs. The lens can be delivered with this instrument.

In preparing the instruments for use in an operation duplicates of each are placed in a metal box, which contains a maximum thermometer, and sterilized in Luer's heat sterilizer for half an hour at a temperature of 130 C. They remain in the metal box until the operation is begun. I introduced the sterilization of instruments by dry heat twenty-five

years ago and observe with pleasure that this method has recently been winning the favor of many surgeons.

Accessories and dressings are autoclaved at a temperature of 110 C., under a pressure of 0.5 atmosphere.

A Hess-Hammer (Zeiss) lamp is employed for the illumination of the field of operation.

PREPARATION OF THE PATIENT

A thorough examination of the patient is made preceding the operation. The age of the patient exerts no influence on the outcome of the operation. As to the eye, special attention should be paid to the accessory organs and the surrounding area. The lacrimal duct is syringed in every case, and a microscopic examination of the conjunctival secretion is made. We find the making of bacteriologic cultures in every case superfluous, as the microscopic examination of smears usually suffices to reveal the presence of an increased number of pyogenic and other pathogenic bacteria. If such organisms are detected, the conjunctiva must be treated. Our routine treatment consists of the irrigation of the conjunctiva with a 1 : 10,000 solution of mercury oxycyanide, combined with the instillation of a few drops of 1.5 per cent optochin hydrochloride. In cases in which there is a discharge, a 10 per cent solution of mild silver protein is also instilled; from 1 to 2 per cent solution of silver nitrate is employed only when the checking of an abundant discharge is necessary. Blepharadenitis is treated with an ointment of 5 per cent zinc oxide and boric acid or with 10 per cent bismuth tetrabrompyrocatechinate. In cases of dacryocystitis the lacrimal sac should be removed before the operation.

The immediate preparation of the patient is simple. The eyelids and the surrounding area are thoroughly cleansed with neutral soap, the edges of the eyelashes are brushed with tincture of iodine, and the conjuncival sac is irrigated with a tepid 3 per cent solution of boric acid. We anesthetize with 5 drops of cocaine hydrochloride, specially prepared for anesthesia, the first drop being instilled twenty minutes before the operation. One drop of a 1 : 1,000 solution of epinephrine hydrochloride and 1 drop of a 1 per cent solution of atropine are instilled immediately before the operation, the latter exerting its effect only after the operation. During the operation we are satisfied with the mydriasis produced by cocaine and do not want the spinchter pupillae to lose its contractility. The use of antiseptics is avoided. In general, we lay special stress on the gentle manipulation of the tissues, and on the gentle touch of the operator's hand.

After the necessary preparations are finished, the patient is placed on an operating table of the Hirschberg type, and a linen cloth, with

a large enough opening in it to leave the field of operation uncovered is placed over the face.

TECHNIC

The operator stands at the right of the patient. Following Arlt's method—I consider myself as a grandson of Arlt's school, my teacher having been his assistant—we are trained to use either hand, i. e., to make an incision in the right eye with the left hand or in the left eye with the right hand.

For steadying the eyeball, we use the method of thread-fixation in every case, according to Angelucci's principle; and following the advice first expressed by Blaskovics and later by Elschnig, retrobulbar injection of procaine hydrochloride combined with epinephrine, effecting akinesia and orbicular paralysis, is employed in every case.

Extracapsular Method.—Special attention should be paid to precision of technic. The incision is made in that part of the limbus which corresponds with the upper third of the cornea. When completing the incision, a small conjunctival flap is also secured. A small fold of the iris is then grasped and excised with one sweep of the scissors. This is followed by catching a large part of the capsule with Schulek's forceps, and thus effecting its rupture. Expression of the lens is accomplished finally with a Daviel spoon. A great advantage is rendered by the use of capsule forceps, as they remove the larger part of the anterior capsule which is behind the pupillary area. After the expulsion of the lens, the removal of the remnants is carried out with the Graefe spoon, assisted by the Daviel spoon.

This method of operation has been in general use for many years. The results have been satisfactory, no remnants being left behind after operation on mature and hypermature cataracts. The remnants of the cortex left behind after the removal of immature cataracts were absorbed in most cases. Postoperative complications were confined to the cases in which irritation or inflammation of the iris occurred after the operation. The occurrence of such complications can, by careful technic, be reduced to a minimum.

Intracapsular Method.—A general attempt is being made at the present time to remove the lens while still in the capsule.[1] I realized the advantages of such an operation twenty-five years ago, but I was also aware of the disadvantages involved. Having often succeeded in removing the lens in the capsule when using Schulek's forceps in cases of hypermature senile cataract, I made an attempt to increase the chances for such an extraction, and a type of Schulek's forceps was used that had

1. Herman Knapp wrote to Henry Smith on Feb. 6, 1905: "If you can establish a safe method of intracapsular extraction of cataract, you will be a greater benefactor to mankind than Daviel."

no teeth at the end of the blade. The introduction of this change also enabled us to deliver the whole lens with the capsule in the mature stage of the cataract. Retrobulbar injections were not employed in those days, and thread fixation and akinesia were also unknown; accordingly, the fundamental conditions required for the efficiency of such an operation were missing.

Under such conditions the extraction of the lens in the capsule was successful in only from 20 to 30 per cent of the cases. However, the percentage of successful operations increased from month to month after retrobulbar injection, consecutive akinesia and thread fixation were introduced. At the beginning, the proportion of satisfactory operations increased from 26 to 44 per cent; at present it has reached an average of 60 per cent. If the cataracts primarily contraindicating this method are excluded, the frequency of successful operations rises to 80 per cent. Most of my operations for cataract are combined with iridectomy, for which I prefer to employ the direct method rather than the one suggested by Knapp and Elschnig. The danger of spontaneous rupture of the capsule and prolapse of the vitreous is greater when the latter method is used than with the direct procedure, which can be completed in the usual way even if this complication occurs during operation. There is no doubt that those who operate with a round pupil display, in delivering the lens, the courage of a *salto mortale*. I used to employ this method, but I reached the conclusion that the basal excision of the iris, according to Hess, or the incision suggested by Elschnig, does not altogether eliminate the dreaded postoperative prolapse of the iris and that it prevents the displacement of the pupil even to a less degree. The successful extraction of the lens while still in the capsule and the simultaneous conservation of a round pupil appear, beyond doubt, to be an ideal method; but when choosing between alternatives, I am always led by the principle that the primary aim is the return of good vision in as many cases as possible, without the risk of complications. Ninety-nine per cent good results are preferable to 95 per cent beautiful results. The loss suffered by 4 per cent of the patients is by no means balanced by the satisfaction of 95 per cent of them.

The method employed by me, and by my pupils, for many decades was further developed and reported on by Erwin Török, and it is now named after him. This gives me special pleasure, and my only desire would be to see it spread as the "Hungarian method," analogous to the plastic operations on the eyelids introduced by Blaskovics and Imre, which are known as Hungarian ways of procedure. A description of the method was given by Török in his book entitled "The Surgery of the Eye," and it was also mentioned in Elschnig's monograph published in 1932. Accordingly, I confine myself to making brief comment on the subject.

The extraction of the lens in its capsule is considerably promoted by the application of retrobulbar injection, akinesia and thread fixation. The larger part of the wound is made in the limbus, and a fairly large conjunctival flap is also secured. Iridectomy is performed with one sweep of the scissors, and because the sphincter pupillae is not paralyzed, the free pillars of the coloboma spontaneously slip into their proper place. The capsule is grasped in the area of the coloboma corresponding with the upper third of the lens, and the extraction of the lens is accomplished with the forceps, which is assisted by a push with Schulek's expulsor applied on the lower limbus. The disadvantage of this method is said to be the more frequent occurrence of prolapse and consequent loss of vitreous. My own experience does not confirm the truth of this statement. The proportional occurrence of prolapse of the vitreous has always been low in our clinic; the main reason for this lies in the continuous endeavor of my associates and myself to emphasize the necessity of the most careful and gentle manipulation during operation for cataract. This endeavor has been greatly helped by the use of retrobulbar injections, akinesia and thread fixation.

The losses of vitreous that we met with during extractions of the lens with the capsule were no higher than those obtained when we employed the extracapsular method. The difference was but 2 per cent in the old days, and was recently reduced to from 1.8 to 1.5 per cent.

Two and three-tenths per cent of 5,000 cataract operations have been complicated by losses of vitreous in the last ten years (thirty years ago this complication was twice as frequent). A decreasing tendency is still further observed in these figures, as from 1923 to 1927 we encountered loss of vitreous in 2.6 per cent of cases, whereas in the period from 1928 to 1931 the rate of occurrence was reduced to 1.7 per cent. Further improvements may be expected from the hypotonia produced by retrobulbar injections.

In spite of the present favorable survey, the further results of intracapsular removal of cataracts must be followed up for many more years, and experience will reveal whether any postoperative disadvantages are to be discovered.

AFTER-TREATMENT

Both eyes are bandaged for twenty-four hours. On the second day, the bandage is changed and the eye not operated on is left open. If the patient is restless, or is apt to be nervous, the bandage may be removed from this eye after twelve hours. Should the patient complain of pain in the eye that was not operated on it is cleansed with warm 3 per cent boric acid solution. By the removal of the retained secre-

tion, this will afford great relief. Six hours following the operation the patient may sit up in bed, and should he complain of headache, he is allowed to sit up in an armchair for twelve hours afterward. We never keep our patients in bed longer than twenty-four hours.

To prevent injury to the eye or rupture of the wound, Fuchs' wire mask is applied on the second day following the operation. It is placed over a bandage at first, but after four days the bandage is removed. After the first week the patient wears smoked glasses, and he is kept in a slightly darkened room to avoid direct sunlight. The pupil is dilated by instilling a 1 per cent solution of atropine. As a rule, the patient may leave the hospital two weeks after the operation, examination of the vision being made to see whether the results are satisfactory. Having once left, some of our patients fail to return for another examination, but those who do are examined four or six weeks later; the acuity of their vision is determined, and glasses are prescribed for them. The astigmatism caused by the wound usually averages about 2 diopters, but sometimes it may be higher. It may be increased by the greater size of the wound and by the laxity of after-treatment. The Gullstrand glasses prove to be very beneficial, as they prevent the distortion usually produced by the use of the required cylindric glasses. Count Stephen Tisza, Hungary's well known prime minister, wearing "punktal glasses," fought four duels with the sword after having been operated on for cataract; he wounded all of his adversaries, while he himself was uninjured. If the healing process is not disturbed by complications, most patients can wear their glasses in two weeks, and they can return to their routine of living without running any risk. One of Hungary's former prime ministers, Count Khuen Héderváry, took part in a political banquet two weeks following his operation without feeling any unfavorable after-effect.

RESULTS

Among postoperative complications, rupture of the wound is most frequently encountered. Paracentesis was necessitated in 4 per cent of these cases. The comparatively frequent occurrence of this complication may be explained by the fact that a great number of the patients admitted to our clinic belong to the less intelligent lower classes; consequently they are not accustomed to discipline and self-control, and they are apt to be unruly. Patients coming from the middle class have had their nerves greatly affected by the World War, revolution and subsequent economic upheavals. These conditions seem to have induced Blaskovics to suggest the securing of Kuhnt's conjunctival flap in every extraction of a cataract. However, this procedure considerably prolongs the time of operation, and I am not convinced of its necessity.

The rate of occurrence of postoperative inflammation exhibits a tendency to decrease. Much to my regret, no operator is able to eliminate the occasional occurrence of failures, nor can he entirely avoid postoperative inflammation. The latter complication is partly due to the lack of means for adequate sterilization of the field of operation.

Nevertheless, when taking into consideration that Jung Shilling, in his book published in 1791, recorded failures in 14 per cent of 2,000 extractions of cataracts and that Daviel himself operated with a 12 per cent, and Arlt with a 5 per cent, loss, our 0.5 per cent of failures may be regarded as the result of considerable progress in the domain of cataract extraction. This 0.5 per cent of unfavorable outcome is mostly due to infection which occurred in spite of the application of all necessary preventive measures.

Thirty years ago the frequency of unfavorable results amounted to 3 per cent, and we succeeded in decreasing the rate of occurrence only by degrees. Ten years ago we met with a 1 per cent loss; in the last five years this incidence decreased to 0.6 per cent, and in 1932 it was but 0.48 per cent. Our principal endeavor is the further reduction of these figures. It must be borne in mind, however, that a great number of the patients entering our clinic come from the poorest classes, and large numbers of bacteria are accumulated in their conjunctival secretions. In figuring the proportion of our failures, all operations are included which have been performed in the clinic, regardless of whether I did them myself or whether they were done by my assistants. It is to be admitted, however, that the results obtained by my assistants are about identical with my own, the training of my assistants in operations for cataract being carried out by degrees. By the time their turn comes actually to operate on a cataract they are sufficiently skilled in technic; moreover, some of them are naturally skilful in operation. This system of gradual training has created such a good reputation for the University Ophthalmologic Clinic that people from all over the country come here to have their cataracts removed.

Ophthalmologists have reason to be proud of the fact they were the pioneers in asepsis and local anesthesia. At the time when 96 per cent of the patients operated on by general surgeons died of sepsis, ophthalmologic surgeons had 5 per cent of infections. The further reduction of our 0.5 per cent incidence of infections necessitates the utmost care and attention; its entire elimination, however, cannot be hoped for at the moment.

So-called expulsive hemorrhage is rarely met with. In the last ten years we have experienced it in 4 instances in 4,994 extractions of cataracts; thus more than 1,000 cataract operations involve the risk of the occurrence of 1 expulsive hemorrhage.

Operative intervention for secondary cataracts is comparatively rarely asked of us. The majority of our patients consist of farmers who are satisfied with vision of from 5/15 to 5/20. Operation on secondary cataract, whenever necessitated, is performed with Kuhnt's knife and consists of subconjunctival penetration into the limbus at the thinnest spot. This method enables us to overcome the danger involved in incision. I experienced no loss in 350 cases. The acuity of vision increased fiftyfold in 15 cases, fifteenfold in 28, eightfold in 90, and fourfold in 94. Vision was doubled in 61 cases, and only 17 operations (5 per cent) produced no result.

My views in regard to the indications for operative intervention for senile cataract are as follows: It is advisable to wait for the maturation of senile cataracts. With immature cataract in one eye and good vision in the other, the cataract should not be operated on. If the cataract in one eye is mature and the other eye is unimpaired, and if the patient displays general good health, the cataract should be removed, for the hypermaturation of the cataract in later years may be accompanied by unavoidable complications (iridocyclitis, secondary glaucoma). Should senile cataract develop in both eyes, the social condition of the patient often makes it necessary to operate before maturity. The presence of fairly good vision, however, contraindicates the performance of such an operation.

The most appropriate stages at which to operate with the intracapsular method are those of maturity and hypermaturity. Operation may be performed before the swelling of the lens, as the swelling makes the capsule fit too tight and the smooth blade of the forceps slips off the lens. Nevertheless, the extraction of the lens with the capsule is most necessary in this stage.

In Morgagnian cataract the removal of the lens in the capsule involves difficulties, but the small nucleus and the opaque cortex can be removed easily through the opening made on the capsule with a tooth forceps.

Luxated lenses are usually removed with Graefe's spoon, for extraction with forceps is rarely successful. Operation should never be performed on both eyes at one sitting, as the absence of vision in both eyes may mean a serious strain on the patient's nerves.

The final conclusion drawn from these statements is that experience gained during the performance of numerous operations induces the operator to be conservative.

In conclusion I quote the words of Arlt, the great ophthalmologic surgeon, and suggest that his warning be borne in mind whenever one is faced with the problem of operation for cataract: "Salus aegroti suprema lex" (The welfare of the patient is the supreme law).

SCLEROMALACIA PERFORANS

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There is not a great variety of disease of the sclera. In this respect, there is a great difference between the two parts of the solid tissue of the eyeball—the sclera and the cornea. So many different diseases of the cornea are seen that it is nearly impossible to make a good classification of them.

Leber based his standard work on inflammation principally on his experimental research on inflammation of the cornea, in which the various stages of the disease can be followed so easily in the clear and transparent tissue. Leber's work gives one a good understanding of inflammation, so that one has a good classification of the types of inflammation in the lungs, the liver and other organs, but unfortunately not of the cornea. In a way one is able to see too much in this tissue, and the symptoms are too numerous to master. As soon as one thinks one knows a good deal about a certain disease, new methods of examination are invented which show other details, and these sometimes change one's conception of the condition. So it was when the corneal microscope was invented, and still more so when that splendid instrument, the slit lamp, was put into use.

I believe that this multiplicity of detail is the reason why the chapter on the cornea in Graefe-Saemisch's "Handbuch der gesamten Augenheilkunde" has not yet been printed, although publication has already taken thirty-five years, and that it will be several years before the results of investigations on the cornea will be in a suitable state for a systematic survey.

Another reason why one sees so many more diseases of the cornea than of the sclera is that the cornea is composed of more different parts. The sclera corresponds only to the parenchyma of the cornea. Its anterior portion is covered by the conjunctiva, which is considered a separate anatomic entity, and its interior surface is covered by the uvea, whereas in the cornea conjunctival and uveal tissues are included in a single structure. The fact remains that diseases of the sclera are not manifold in their variety. As a rule, one finds that in the chapter on the sclera in textbooks and encyclopedias only injuries, inflammations, staphylomas and discolorations are mentioned.

The inflammations are almost never ulcerous. Perforation of the sclera except as the result of injury is rare, though a tumor of the

uvea, a gumma or a tubercle of the uvea may grow through the scleral coat. Staphyloma of the sclera may be total, as in infantile glaucoma, in which the sclera bulges on account of the high pressure, or it may be local. Local staphylomas are usually caused by the combination of high pressure and lessened resistance, e. g., in regions of thinning of the sclera due to scars or at the points where the vessels perforate the sclera. Thinning of the sclera alone is, as a rule, not sufficient to cause bulging of the tissue, as in cases of blue scleras. Discoloration of the sclera may be either a true discoloration, as from pigmentation, or a pseudodiscoloration, as in blue scleras and scars, in which the slate blue or gray color is caused by the diffuse spreading in the sclera of the light reflected from the darkly colored uvea.

The disease which I wish to describe here has as its principal symptom the appearance of holes in the sclera, which can coalesce so that the sclera shows large gaps in which the uvea lies either covered by conjunctiva or bare. As far as Professor Rochat and I, who both examined two of these patients,[1] could make out, this disease has not been described heretofore.

It is rather astonishing that even after the eye has been scrupulously studied by the many excellent means of examination for many years, an ocular disease can be described as a new one, in which the symptoms may be easily detected with the naked eye. It is, however, possible that other oculists have also observed cases of this disease, but that they have failed to describe them, as, indeed, Professor Rochat and I did for many years, until other cases of the same type came to our attention and made it desirable for us to give a description.

In this disease inflammation plays no rôle, or at least a very secondary one. The process is more of a degeneration, so that I have given it the name "scleromalacia perforans." How well this name suits the disease is seen from the fact that when I talked about my cases before the Dutch Ophthalmological Society (Nederlandsch oogheelkundig geselschap) in 1930, Professor Rochat, recognizing the condition from the title, showed drawings made from his first case (fig. 2), which appeared to be exactly the same as my first one. Consequently, Professor Rochat,[2] who had first given this disease the name "scleritis necroticans," agreed fully with me that the "scleromalacia" was the better name.

I saw my first case in 1928, when it was presented to me by Dr. W. van Hoorn, an oculist in The Hague.

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1. Professor Rochat has permitted me to publish the reports of his cases.

2. Rochat: Nederlandsch oogheelkundig geselschap, December, 1932; Nederl. tijdschr. v. geneesk. **77**:1935, 1933.

REPORT OF CASES

CASE 1 (author's case).—A woman, aged 55, complained that for many years her vision had been diminishing. She was brought to my clinic with some difficulty, as she could scarcely move on account of the total or partial ankylosis and swelling of a great many of her joints. We thought this might be caused by gout, but examination in the clinic for internal medicine showed that the condition was due to chronic rheumatic polyarthritis, from which disease she had already suffered a great many years.

Degenerative clouding of the cornea at the periphery and almost mature cataract were found in both eyes. The iris, in the small part which could be observed, seemed to be atrophic, but the greatest changes were observed in the sclera. Hyperemia of the bulbar conjunctiva and small and large holes in the sclera of both eyes were seen. Figure 1 shows the condition of the left eye; the right eye was almost the same. The larger holes seemed to have resulted from the confluence of smaller ones. The conjunctiva, as a whole, seemed to be rather atrophic. Over some of the gaps it was still present, covering the uvea completely; over other

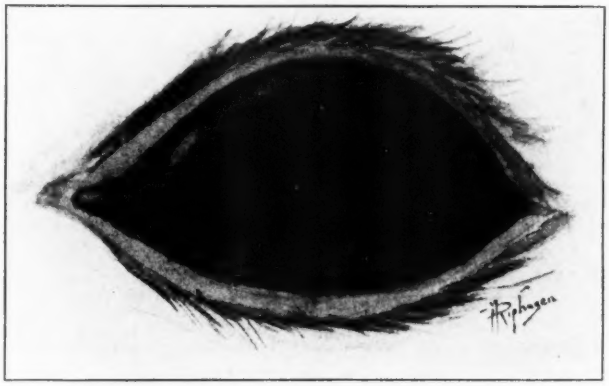

Fig. 1 (case 1).—Scleromalacia perforans.

holes there were only some rags of conjunctiva, and over still others it was gone, so that the uvea lay bare. Dr. van Hoorn told me that sometimes when a hole was being formed, he had seen first a yellowish excrescence below the conjunctiva, appearing like an abscess. However, when this was punctured no pus came out, but only a kind of detritus. Unluckily this detritus has not been examined.

Since I feared that the bare uvea might become infected, as in the first patient of Professor Rochat, I covered every gap with mucosa from the inner surface of the lip, which healed well. Examination of small parts of the sclera removed at this operation revealed degeneration or chronic inflammation. Visual acuity was poor; in the right eye there was only perception of light with good projection, and in the left, vision of 1/300.

I first extracted the crystalline lens of the right eye, and later that of the left, which improved the visual acuity a little. The excised part of the iris showed atrophy on microscopic examination. Some years later the patient died, but the eyes could not be obtained for examination.

CASE 2 (Professor Rochat's first case).—An old woman was seen in 1925, with all the joints both of the trunk and of the limbs more or less ankylotic, so

that she could not move. In the clinic for internal medicine the diagnosis of arthritis deformans, without gout, was made. The general condition was, therefore, the same as in my first case. The condition of the eyes was so much like that in my case that Professor Rochat expressed himself in these words, "the ocular conditions resembled each other as do two drops of water."

The ocular condition had already lasted a long time, and large holes were found in the sclera; the cornea were more or less opaque. The only difference in our two cases was that the bare uvea in Rochat's patient had become infected, so that the eyes were inflamed, and in both anterior chambers a huge hypopyon was present (fig. 2). The patient was blind.

CASE 3 (Professor Rochat's second patient).—This patient, a woman, aged 54, was seen in 1932 in an earlier stage of the ocular process. There was ankylosis of almost every joint in the body. Figure 3 shows the condition of the hands, which was the same as that in cases 1 and 2. The disease began ten years previously with an attack of acute rheumatism, and was diagnosed at the clinic for

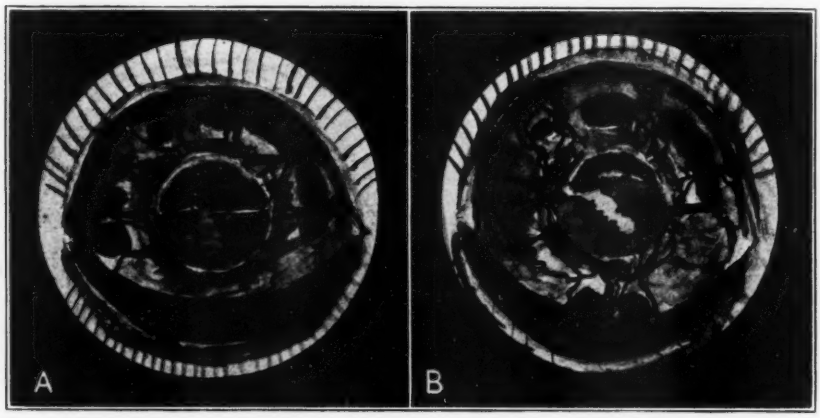

Fig. 2 (case 2).—Drawings made in Professor Rochat's first case.

internal diseases in Groningen as chronic rheumatic polyarthritis, as in the other cases. In addition, the patient had diabetes. Big holes were found in the sclera in which the uvea lay bare, but there were no other changes in the eyes (fig. 4). There were no symptoms of inflammation; the corneas and crystalline lenses were clear. On examination with the slit lamp there was no sign of iritis or cyclitis. While the first two cases had made it seem highly probable that the disease begins in the sclera and not in the uvea, this case gave the real proof. So, also, the fact that in my case some of the holes were still covered by conjunctiva shows that the beginning of the disease is not to be looked for in the conjunctiva but in the sclera, and there only. It was remakable that in these cases the uvea did not bulge out of the holes. This was probably caused by the fact that the tension of the eyes was normal, and proves that under certain conditions the uvea can bear the pressure of the eye without the help of the sclera, or that the bare choroid allows enough fluid to pass out to prevent bulging. Figure 5 shows a stereoscopic photograph of a hole in the sclera of my patient. No difference can be seen between the stereoscopic photographs which Professor Rochat made of his second patient, and those of my patient.

Fig. 3 (case 3).—Appearance of the hands in Professor Rochat's second case.

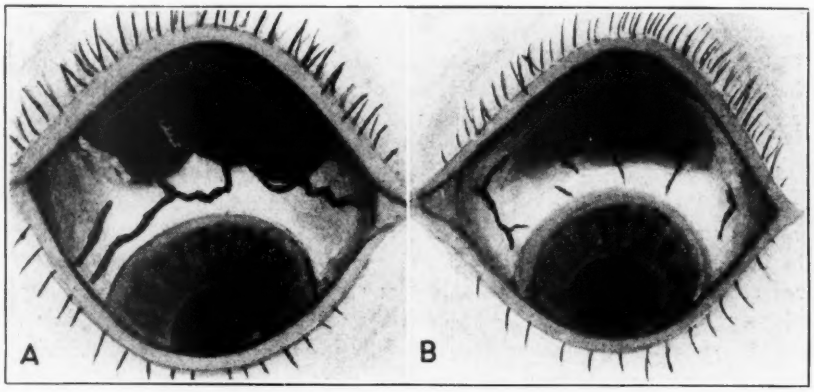

Fig. 4 (case 3).—Holes in the sclera in the patient shown in figure 3.

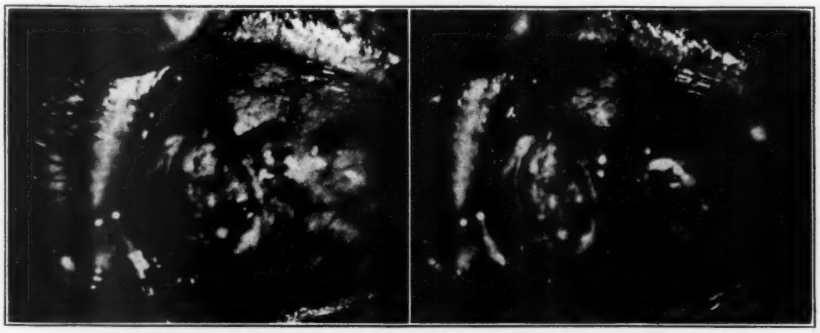

Fig. 5 (case 1).—Stereoscopic photographs of a hole in the sclera.

It is clear, therefore, that the condition described is a characteristic disease entity.

In patients with chronic rheumatic polyarthritis, degeneration of the sclera occurs with negative bacteriologic findings, which results after a time in the development of holes of varying size in the sclera, over which the conjunctiva may be present, atrophic or absent. Secondary clouding of the cornea and infection of the uvea may ensue.

The holes are not restricted to a special part of the sclera, but could be found in these three cases from the limbus to the equator. It was not possible to determine whether they were also present in the posterior part of the sclera.

In the cases so far reported the only part of the sclera in which no hole was present was the intercalary portion where the sclera is a part of the wall of the anterior chamber. What happens when a hole develops in this portion was shown by my second case, which was remarkable.

CASE 4 (author's case).—In 1931, a man, aged 69, was sent to me by his doctor, who had perceived something abnormal in both eyes. The patient had never been ill, had four healthy children and had never had any symptoms of rheumatism. He said that forty-eight years previously, as a young man of 21, he had had an ocular inflammation, which had not been seen by a physician. He had had pain and redness in both eyes. These symptoms had recurred nearly every week for thirty years, but during recent years there had not been any pain. The patient knew that he had a black spot at the top of his left eye, but though he was living at a distance of only 4 miles from the ophthalmic clinic at the university in Leyden, he had never thought it advisable to go either to his doctor or to the clinic until recently, when he began to see a spot, like a fly before his eye.

The result of the examination was remarkable. Both eyes were absolutely quiet, with normal tension. Visual acuity of the right eye was 6/10 with cyl. +2 axis 60° temporal = 9/10. Visual acuity of the left eye was 2/10 with cyl. +2 axis 45° nasal = 4/10. The fundus oculi was normal, except that there were some drusen in the choroid.

The cornea of the left eye (fig. 6*B*) showed clouding of the periphery and a rather thick arcus senilis; above in the cornea could be seen a large white patch which consisted, as did also the greater part of the arcus senilis, of crystals, which, on examination with corneal microscope and slit lamp, gave one the impression of being urate crystals. Above the cornea a black tumor was seen which was formed by a prolapse of the subconjunctival iris through a small fissure in the sclera.

In the right eye (fig. 6*A*) the periphery of the cornea was clearer; the arcus senilis was not so thick as in the left eye, but nevertheless showed the same crystals. At the nasal side of the cornea was found a subconjunctival cyst, and through the semitransparent cyst one could see a vertical fissure in the sclera just next to the limbus. The whole lesion looked like a filtering scar after a Lagrange operation at an unusual location; in fact, it was the prototype of a filtering scar. Since the patient did not have much trouble with his eyes, and since the condition seemed to have been present for a great many years, I held myself to the sound principle: Wait and see what happens.

The patient was examined in the clinic for internal medicine, but no signs of change in his purine metabolism were found. Nevertheless, I thought of the possibility that the crystals in the corneas were urates, and that this was a case of monosymptomatic gout. After a couple of months, the aspect of the left eye changed; the prolapse increased a little, and at one spot the conjunctiva was perforated, so that the iris became bare.

Now I thought it was time to act. I loosened the conjunctiva from the iris, excised the prolapse, found the hole in the sclera and removed a part of the sclera and cornea containing crystals for examination. The gap was covered with conjunctiva and healed in a short time. I punctured the cyst on the right eye and emptied it with a Pravaz syringe. Immediately one could see the fissure in the sclera much better than before. In a couple of days the cyst filled again, and the condition remained as before.

The microscopic examination of the small particles of cornea and sclera showed degeneration, but no signs of inflammation. The crystals proved to be not uric acid but cholesterol. This was, therefore, not a case of monosymptomatic gout, but again a somewhat peculiar case of scleromalacia perforans.

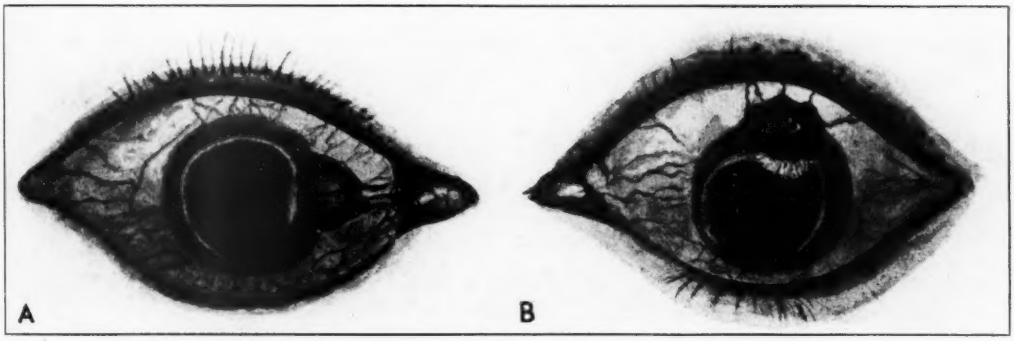

Fig. 6 (case 4).—Appearance of right (*A*) and left (*B*) eye in an unusual case of scleromalacia perforans.

COMMENT

I do not believe that these interesting cases are as rare as they seem to be. At the meeting of the Dutch Ophthalmological Society where this condition was discussed, Dr. Otto Roelofs and Dr. Winkler Prins both told about a case in a patient suffering from rheumatic arthritis which seemed to belong to the group described. Moreover, Dr. Winkler Prins told about a case of scleromalacia in a patient without rheumatism.

Concerning the sex incidence not enough patients have been seen to decide whether the female or the male sex prevails in this disease. In the cases with rheumatic polyarthritis, the three patients were all women; Dr. Roelofs' patient was also a woman, but the patient of Winkler Prins was an old man. The cases without polyarthritis were both in men. Concerning the age incidence, it seems that the condition is more prevalent in middle age and old age, but from the slow onset

and the long duration of the disease, e. g., in my cases without rheumatism, it is rather difficult to say whether the beginning is in youth or in later life. Perhaps two types of scleromalacia may be distinguished, one with, and the other without chronic rheumatism. It is not astonishing that a combination of disease of the joints and of the sclera can exist, for disease of the sclera are found in patients suffering from diseases of the bones and joints. Acute or chronic rheumatism is often accompanied by scleritis; diseases such as tuberculosis, syphilis and endogenous gonorrheal infection can affect several joints as well as the sclera; in the well known syndrome of blue scleras the scleral condition is associated with brittle bones.

In scleromalacia, it is possible that one has to distinguish two different types of cases: (*a*) those connected with chronic rheumatic arthritis and (*b*) those occurring without this disease. But it may be that these two types have the same cause, a constitutional predisposition both to polyarthritis and to scleromalacia, so that the symptoms of both conditions may occur together or those of polyarthritis or of scleromalacia alone.

But here one comes to the realm of hypothesis, in which not enough is known about this remarkable disease to proceed. One does better to keep to the bare facts: that there can be distinguished a typical disease of the sclera which consists in the appearance of various-sized holes in the sclera without dominant signs of inflammation, often accompanied by rheumatic polyarthritis, and for which an appropriate name seems to be scleromalacia perforans.

PATHOLOGY OF TUBERCULOSIS OF THE ANTERIOR UVEA

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The time has passed when the epithelioid tubercle was the only reliable witness to tuberculous infection, though this still remains the principal histologic proof of tuberculosis. The bacillus of tuberculosis, like every other parasite, causes inflammation under certain conditions. Its favorite localization is the vascular apparatus and the connective tissue; hence its special predilection for the uvea. The intensity and course of the tuberculous inflammation depend on the number and virulence of the bacilli and on the reaction of the organ attacked.

The following are examples of the different types of histologic reactions to the invasion of the tubercle bacillus: If tubercle bacilli are injected into the blood vessels of rabbits (Stock [1]), choroiditis and iridocyclitis result; the lesions consist at first only of lymphocytes; gradually epithelioid cells develop, and occasionally giant cells.

A totally different reaction is caused if tuberculous rabbits are superinfected by the introduction of tubercle bacilli into the anterior chamber. An acute, intense, absolutely nonspecific inflammation arises, in which leukocytes and fibrinous exudate are dominant. Nearly all the tubercle bacilli are destroyed, but a typically tuberculous tissue develops in relation to the few remaining bacilli.

A further example is Boeck's sarcoid, which can now without doubt be regarded as tuberculous. In its typical form it consists of pure tuberculoid tissue, without demonstrable tubercle bacilli. However, Kyrle [2] and others succeeded in finding Koch's bacilli in a very early stage of this disease, and it is in this stage that one finds a nonspecific histologic picture. These examples show that the same type of bacilli may cause entirely different pathologic changes under varied circumstances.

On account of this variation in histologic reaction, it would be of great importance if the demonstration of tubercle bacilli in tissue were more successful than it has hitherto been. Löwenstein's [3] new method offers great hope. It must be admitted, however, that his method has not yet been generally accepted, and that therefore the results obtained by it have to be taken with a certain reserve, interesting as they are

1. Stock: Arch. f. Ophth. **66**:51, 1907.
2. Kyrle: Arch. f. Dermat. u. Syph. **125**:481, 1920.
3. Löwenstein: München. med. Wchnschr. **78**:261, 1931.

(Meller [4]). Animal inoculation for the demonstration of the bacilli is not generally applicable, and this test also is often disappointing. Finally, if one attempts by pathologic study to determine the importance of tuberculosis as an etiologic factor in iridocyclitis, one soon concludes that only through the combination of clinical and anatomic findings can one give an answer to this question.

The material for my research comprised cases reported in the literature in which a histologic examination had been made and in addition fifteen cases that I [5] observed. These cases, in which tuberculosis was either proved or suspected, can be separated into three groups: (*A*) acute and subacute types; (*B*) chronic and recurrent types, and (*C*) special types.

A. Clinical observations generally suffice for a positive diagnosis of tuberculosis of the iris of the acute and subacute types. In brief, these cases have the following characteristics:

1. They affect principally persons under 20 years of age.

2. They nearly always affect but one eye.

3. The duration of the disease is generally several weeks or months, at most one year, without any intervals free from inflammation, and the case terminates either in cure or in enucleation.

4. The anterior and posterior chambers are often markedly affected, but the other tissues of the eye (the choroid, retina and cornea) are rarely involved and, if so, only in a mild form.

5. In no other type of tuberculosis of the anterior uvea is it so regularly the rule to find the characteristic histologic tubercle. The anatomic diagnosis, therefore, is nearly always unquestionable.

6. Besides the specific elements (epithelioid and giant cells), lymphocytes and their modifications (plasma cells, macrophages) preponderate. Now and then one finds also a leukocytic reaction.

7. The more acute the process, the more frequently one finds leukocytic elements (hypopyon), caseation or a markedly progressive spread and finally perforation of the globe.

8. Tubercle bacilli are often, but not always, demonstrable in these cases. In two of my own three cases, the bacilli were found mostly in regions of caseation.

B. In contrast to the acute and subacute cases, the chronic and recurrent types of the disease have the following characteristics:

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4. Meller: Ztschr. f. Augenh. **79**:95 and 110, 1932.

5. In this paper I shall give only a summary; for details, I refer to my report presented at the Fourteenth International Ophthalmological Congress in Madrid, Spain.

1. They affect mostly adults and only occasionally children.

2. Both eyes are nearly always involved.

3. Typical epithelioid cell tubercles are not regularly found. Caseation or other necrosis is extremely rare; perforation of the eyeball hardly ever occurs.

4. Other parts of the eye often participate in the disease process of the anterior uvea, in which case the retina, choroid, cornea and sclera may be affected singly or in combination.

5. The chronic inflammation often shows more or less tendency to organization. There are, however, cases of very long duration in which the proliferation of connective tissue is minimal.

6. Tubercle bacilli are rarely found either microscopically or by animal inoculation.

One is seldom able to examine the chronic-recurrent cases histologically at the beginning or even at the climax of the disease. Enucleation is generally performed, not because of the tuberculous process, but because of secondary conditions (glaucoma, detachment of the retina, etc.). In spite of this, pathologic investigation is of importance not only for a better understanding of the individual case, but also for the study of the whole disease process. Now and then, on histologic examination of eyes which have previously undergone tuberculous iridocyclitis, one finds no nodules in the anterior uvea, or at most scattered epithelioid cells, lymphocytes and plasma cells, while in other parts of the eye there may be small, hidden nests of epithelioid cells. Should these nests be overlooked, one might easily be inclined to regard the whole condition as nontuberculous. One can readily understand that these cell nodules, even if they are in the ciliary body or in the deeper layers of the iris, will escape clinical observation.

There are still other cases in which the clinical course appears definitely that of tuberculosis, but in which, histologically, no characteristic changes, either in the uvea or elsewhere in the eye, can be discovered. Here an observation of von Hippel [6] (his case 9) is instructive.

A child of 5 years had chronic iritis with five discrete inflammatory nodules in the iris. Subcutaneous injection of tuberculin resulted in a general and local reaction. The inflammatory proliferations gradually increased and infiltrated the whole iris. Four years later the whole cornea was opaque and the iris atrophic. Histologically, large aggregations of connective tissue were seen at the back of the cornea, as well as nodular infiltrations of plasma cells and round cells in the iris and organization in the deeper layers of the iris and in the posterior chamber, but nowhere was there a sign of specific elements.

To judge from the clinical course, one cannot doubt that this was a case of tuberculosis of the iris. Nevertheless in the old scars there

6. von Hippel, E.: Arch. f. Ophth. **92**:421, 1917.

was no characteristically tuberculous reaction. This shows that sometimes only the combination of clinical and pathologic study can lead to correct judgment.

There remain to be discussed the cases of chronic uveitis in which definite evidence of tuberculosis cannot be found either clinically or histologically, but in which tuberculosis is nevertheless suspected. In Germany the number of these cases is reckoned as very high. In other countries, especially in the United States, most of these cases are attributed to "focal infection." My point of view, based on pathologic studies, is as follows: If one has the rare chance to examine histologically an early stage of iridocyclitis and finds no specific changes, one will have to leave the etiologic diagnosis in suspense and regard tuberculosis as improbable if the clinical appearance is in no way suggestive of tuberculosis. But if one is dealing with late stages of iridocyclitis, one cannot reject the diagnosis of tuberculosis even if the pathologic condition is absolutely nonspecific.

C. The last group of cases, which I have designated special types, are rare, but of great interest. These cases show in how unusual a manner the eye can react to the invasion of tubercle bacilli.

The first variety is that which begins with intense iridocyclitis, rapidly followed by complete loss of vision. The high degree of visual impairment and the pathologic changes visible in the vitreous and in the deeper parts of the fundus indicate clinically that there are serious intra-ocular complications. On pathologic examination, the lesions of the choroid and the retina are most characteristic. There is more or less extensive infiltration of the choroid with lymphocytes and often also with epithelioid cells, and at times the necrotic areas which distinguish this whole group are present. In other cases, the tendency to necrosis is noted only in the retina, which is destroyed more or less widely. In still other cases, a peculiar layer of epithelioid and giant cells is formed between the retina and the choroid, within which or on the surface of which another layer of necrotic cells may be distinguished. In these cases the retina is detached, and in a large part degenerated. The lesions are often most marked near the ora serrata. It is not necessary to enter into further discussion of these pathologic conditions in the posterior portions of the eyeball, for they have no direct relation to the subject. These cases are obviously tuberculous, but the tuberculous lesion is of somewhat uncommon character, presenting in smallest measure the form of nodules, and in high degree a tendency to necrosis. Concerning the changes in the anterior uvea, one can easily conceive that the exudative processes on the surface are secondary to the process in the posterior portions of the globe. Generally there is a diffuse, and sometimes a localized, infiltration of cells of nonspecific appearance in the ciliary body.

The special interest of this group lies in the remarkable necrotic reaction caused by the invasion of tubercle bacilli. That tubercle bacilli are the cause has been proved, at least in the cases of Kägi, Bergmeister and Schöpfer, as well as in one of my own.

Whether the second variety is to be rigorously separated from the preceding one is doubtful. These cases likewise show areas of necrosis, but the purulent character of the infiltration is the principal feature.

A third variety is represented by the unique observation of Mylius and Schürmann[7] (1929). These authors were able to examine, not only clinically but pathologically, the eyes of a patient with atypical general tuberculosis. They described the lesions in the eyes, and also those in the bones, skin, lungs and lymphatic glands, as generalized sclerosing, tuberculous, large cell hyperplasia, characterized by the appearance of noncaseating submiliary, tuberculoid foci with hyaline sclerosis as the sole evidence of retrogressive metamorphosis.

Reaction of Patients According to Age

Group	Age	Number of Patients	Caseation or Necrosis	Hypopyon	Perforation of the Eyeball
1.....	1-10	21	15	7	11
2.....	10-20	13	4	1	4
3.....	20-30	17	6	1	3
4.....	Over 40	9	3	1	2

Brief reference must be made to the relation of uveal tuberculosis to the general constitution and to immunity. That these factors are of great importance cannot be doubted. To determine them in an individual case from the pathologic point of view is seldom possible, for too many factors, specific and nonspecific, are to be considered as bearing on the type of histologic reaction. On the whole it is accepted that hyperergia or hypersensitivity in tuberculosis is expressed by an abundant and violent exudation, with or without caseation, and that with increasing immunity more cellular productivity arises. The following results confirm this conception in relation to tuberculosis of the anterior uvea.

In the accompanying table sixty-seven patients with tuberculosis of the uvea examined pathologically are grouped according to age and type of manifestations.

In the first group, which includes the patients from 1 to 10 years of age, a large variety of serious complications was found. Of twenty-one patients, fifteen showed caseation or necrosis, seven hypopyon, and eleven perforation of the eyeball.

In the other groups these complications were found not nearly as often. Epernon,[8] in 1883, referred in general to the fact that severe

7. Mylius and Schürmann: Beitr. z. Klin. d. Tuberk. **73**:166, 1929.
8. Epernon: Arch. d'opht. **3**:485, 1883.

tuberculosis of the iris is more frequent in early than in adult life. Another fact confirms this: In the literature I have found reports of only four cases of tuberculosis of the anterior uvea in infants, and it is of interest that all of these were characterized by severe exudative processes. All of the patients had caseation, hypopyon or perforation, or all three conditions. This is especially remarkable because infants certainly present a very early stage of tuberculosis and there are general pathologic grounds for the view that in the earliest stages of tuberculosis there is an especially high sensitivity to the toxin.

The more one studies the histologic stages of tuberculosis of the uvea, the more one will appreciate the advantages and the dangers of therapy which is directed toward increasing the inflammatory reaction of the tuberculous focus. It can hardly be doubted that the elimination of the tubercle bacilli is brought about by the histiocytic and lymphocytic elements. It is therefore rational that a certain increase of this elimination is favorable to the course of the tuberculous process. It is comprehensible that such an increase of inflammatory reaction can be induced by nonspecific remedies, such as roentgen irradiation, and also by the slightest focal reaction to the injection of tuberculin.

On the other hand, however, too intense and too rapid dissolution may cause caseating processes or hemorrhages because of the too intense effect on the blood vessels. Furthermore, it is clear that every fresh eruption of other foci in the body and every superinfection may have a bad effect on the process in the eye, probably as the result of autotuberculinization. From this point of view, one sees that climatic therapy and improvement of the general condition in the treatment of other tuberculous processes in the body must likewise help in the treatment of the ocular condition.

Histologic examination remains one of the most important means of understanding the pathogenesis of tuberculous processes in the uvea; but more than that, it gives valuable information as to prognosis and therapy. It must be admitted, however, that in uncertain cases one is not always able to solve all enigmas.

As an appendix to this article I am presenting a number of drawings (figs. 1 to 15) which illustrate the pathologic changes of tuberculosis of the eye. The pictures are taken from anatomic specimens of the cases which I reported at the International Ophthalmological Congress in Madrid, Spain, in 1933. Some of the pictures have already been published in the report of that congress, but most of them are printed here for the first time. The pictures were painted in the university clinic of ophthalmology at Göttingen, and they, as well as the anatomic data on most of my cases, were supplied by my former teacher and friend, Prof. E. von Hippel.

Fig. 1.—A specific infiltration of the root of the iris, with little participation of the ciliary body (*i* indicates the iris; *c*, the ciliary body; *a*, the cornea). From this point tuberculosis of the anterior uvea generally seems to begin.

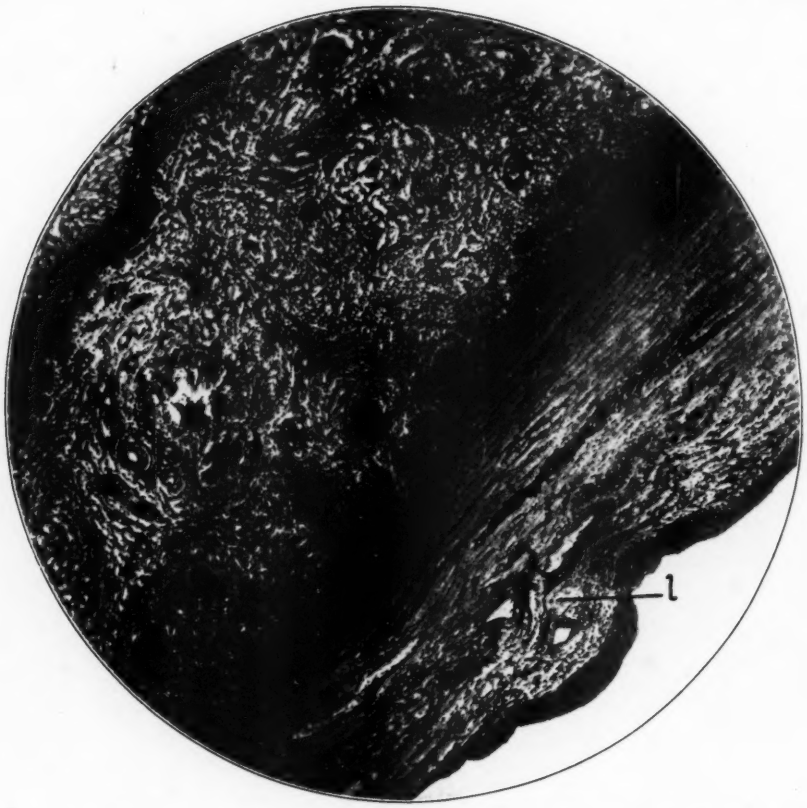

Fig. 2.—Figures 2 to 5 show the development of tuberculosis of the anterior uvea, as it generally takes place (cyclitic type). In this specimen is shown specific infiltration of the iris, with beginning thinning of the sclerocorneal border (*i* indicates the iris; *l*, the limbus corneae).

Fig. 3.—Specific involvement of the ciliary body, with a defect of the epithelial cells and of the layer of pigment in the ciliary body. Typical formation of membranes over the flat part of the ciliary body.

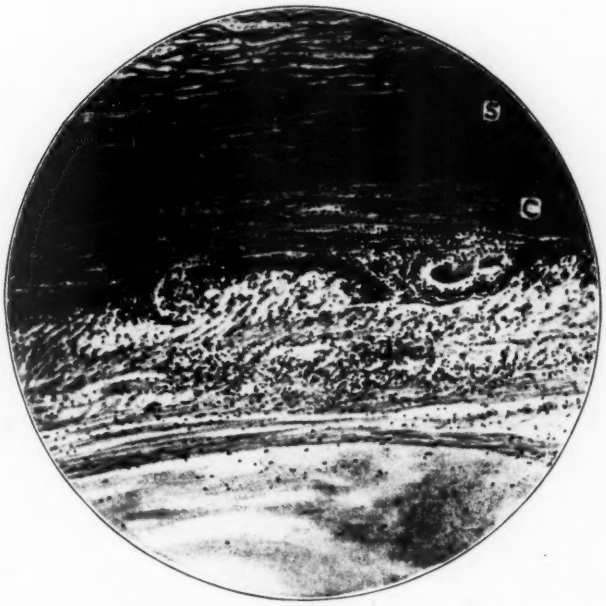

Fig. 4.—Two very small tubercles of the pars plana of the ciliary body beginning to break through the layer of pigment (*s* indicates the sclera; *c*, the ciliary body).

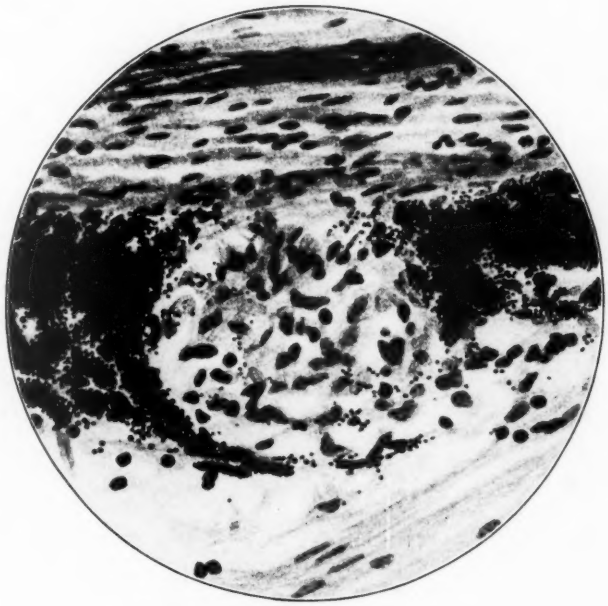

Fig. 5.—Enlargement of figure 4.

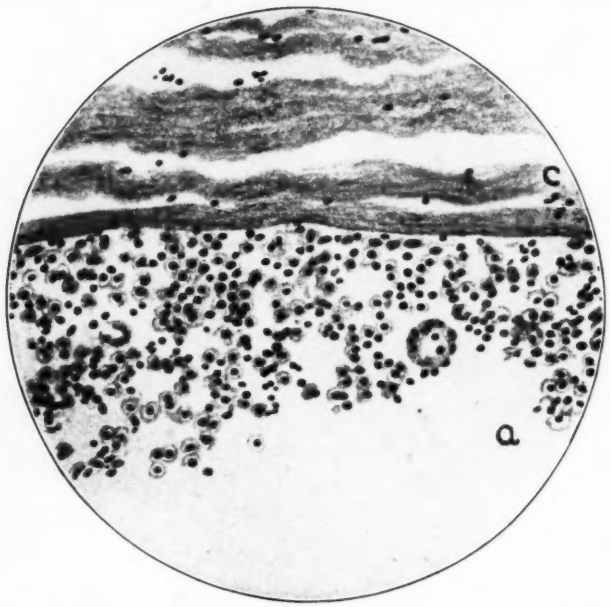

Fig. 6.—Precipitates on the back of the cornea with giant cells (*c* indicates the cornea; *a*, the anterior chamber).

Fig. 7.—Figures 7 to 9 illustrate the rare form of tuberculosis of the uvea, which affects principally the iris and cornea but does not attack the ciliary body (iridocorneal type). This specimen shows typical nodules of tuberculosis in the sclera and limbus, with keratitis tuberculosa.

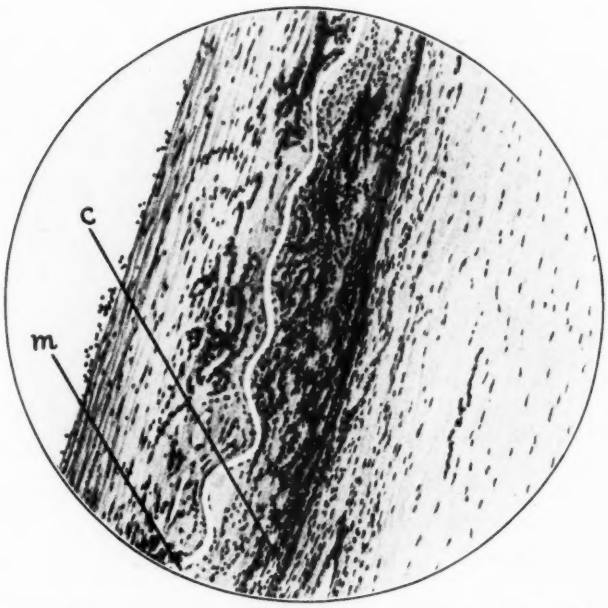

Fig. 8.—Uveitis tuberculosa with keratitis profunda and thickening on the back surface of Descemet's membrane (*m* indicates Descemet's membrane; *c*, the cornea).

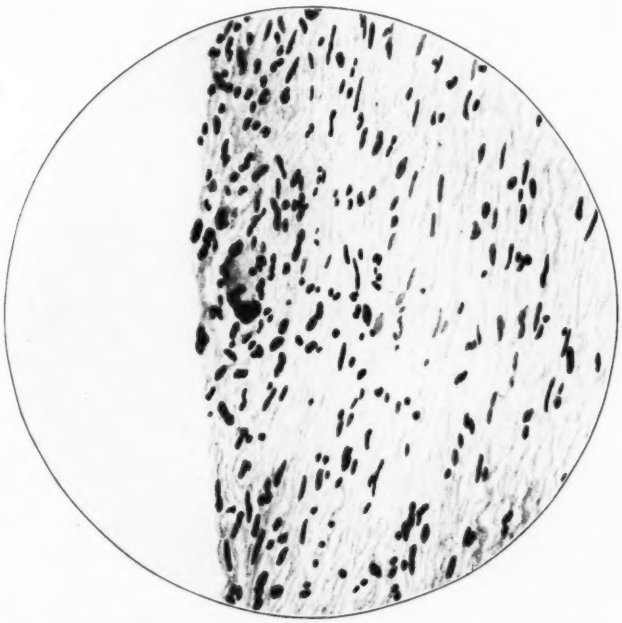

Fig. 9.—Uveitis tuberculosa with keratitis profunda, showing giant cells in a deep infiltration of the cornea.

Fig. 10.—Tuberculosis in part of the root of the iris can also continue via the anterior ciliary vessels into the sclera and conjunctiva, as is shown by this specimen, in which an anterior ciliary vessel is infiltrated.

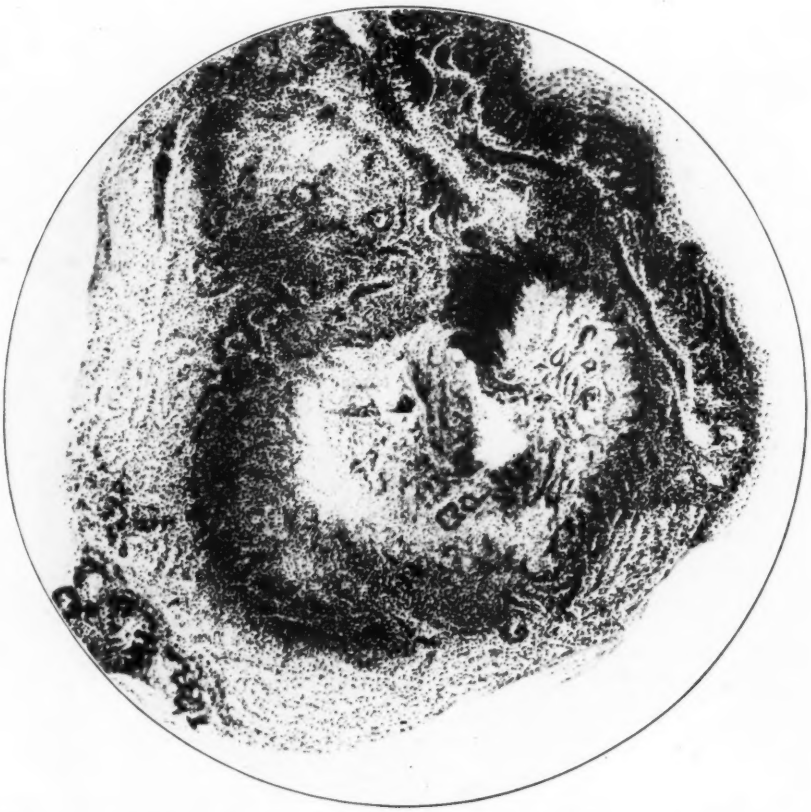

Fig. 11.—Scleritis tuberculosa without participation of the uvea. The specimen shows a nodule with central necrosis. The nodule is surrounded by a ring of epithelioid cells, lymphocytes and giant cells. Koch's bacilli were found.

Fig. 12.—This case appeared clinically to be one of iridocyclitic tuberculosis. Anatomically the infiltration of the iris consists principally of lymphocytes. Moreover, the thickening on the posterior surface of the iris is anatomically not specific. Probably tuberculosis is present, however.

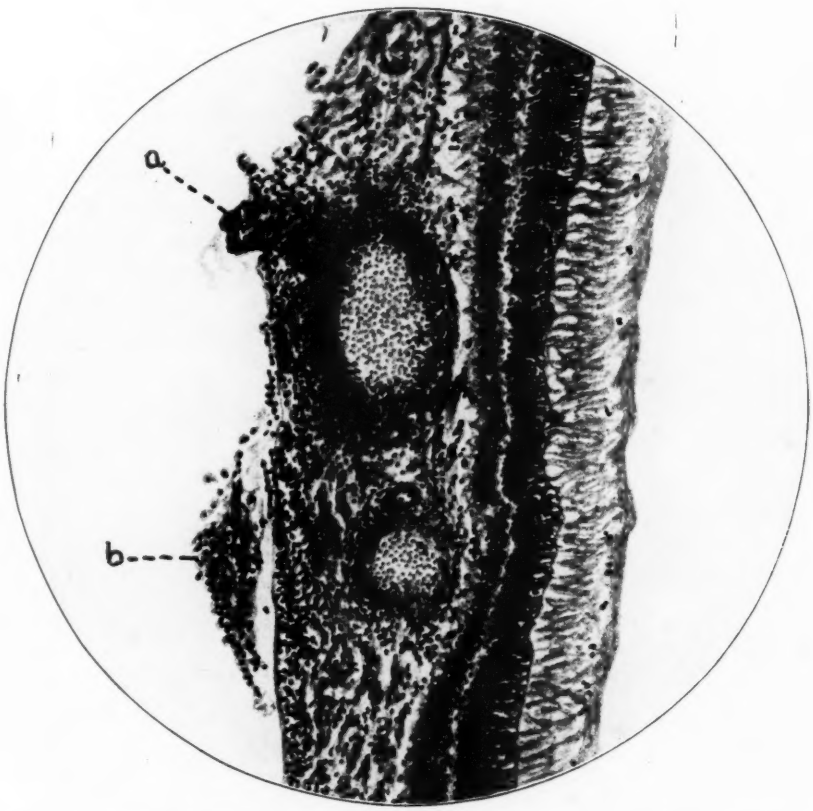

Fig. 13.—Iridocyclitis tuberculosa. Inflammation surrounding the retinal vessels with a small extension through the internal limitive membrane of the retina at point *a* and a tubercle on the inner surface at point *b*.

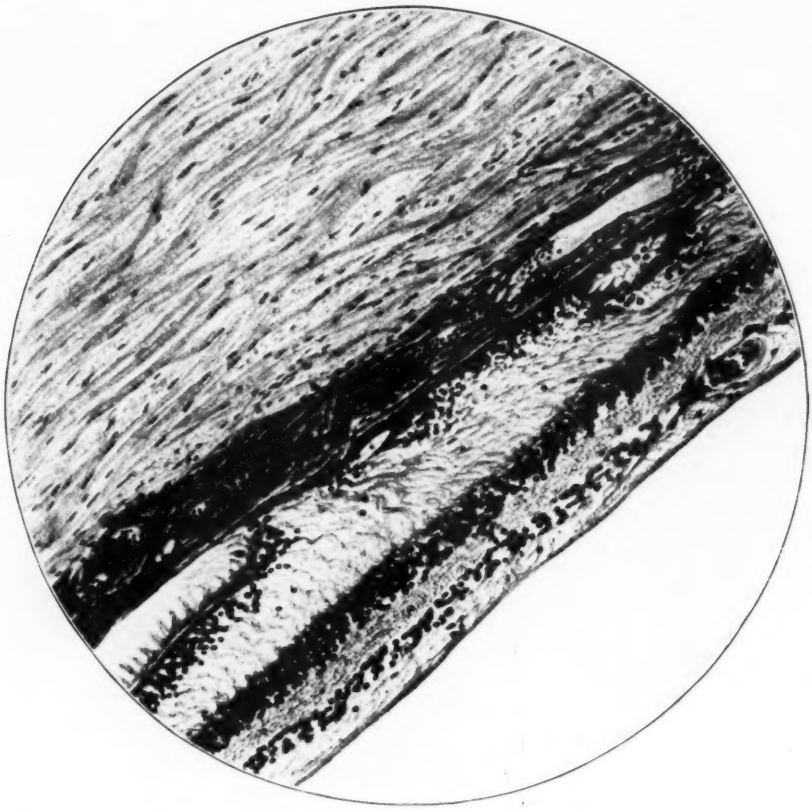

Fig. 14.—Uveitis tuberculosa with keratitis profunda. In this specimen is seen a chorioretinitic spot (infiltration of the choroid, and partial atrophy of the pigment epithelium and the exterior layer of the retina).

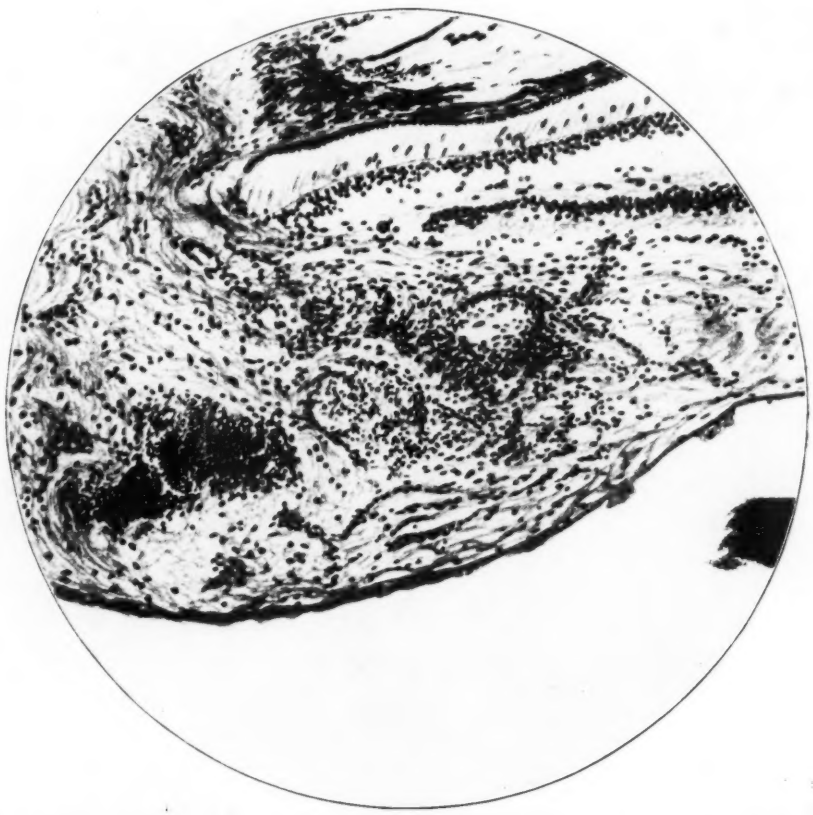

Fig. 15.—Papillitis with perivascular infiltration in a case of uveitis tuberculosa.

CYCLOPLEGIA FOR DIAGNOSIS

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The physiologic action of Hyoscyamus was known to the Greeks. Belladonna, used in a cosmetic during the sixteenth century, probably got its name from the fact that it produced dilatation of the pupil. That stramonium leaves poisoned the early settlers of Virginia, who ate them as greens, gave the plant the popular name of Jamestown (or jimson) weed. From the first moment that these narcotic plants attracted attention, their most striking effect was dilatation of the pupil.[1] The study of their active principles showed that they all contained an alkaloid (or alkaloids) of about the same chemical constitution and of nearly the same physiologic action. In each instance this substance was named from the plant in which it was found: hyoscyamine, atropine, daturine, duboisine and scopolamine; these drugs and the slightly altered derivative of atropine, called homatropine, came to be known as the mydriatic alkaloids or the mydriatics.

The discovery of the ciliary muscle and its function of accommodation revealed the fact that the drugs which dilate the pupil also paralyze the accommodation; that is, they produce cycloplegia. When the importance of accommodation, with the part it plays in modifying and concealing ametropia, was understood, the power of these drugs to produce cycloplegia was found to be more important than their power to dilate the pupil, and, as urged by Casey Wood,[2] they came to be considered and spoken of as cycloplegics. The important use of induced cycloplegia has been in diagnosis, although it may serve a therapeutic purpose, as pointed out by Donders [3] and emphasized by Norris,[4] Risley,[5] Derby [6] and others.

Preparations recognized in the older pharmacopeias have now been replaced by the alkaloids. With the latter, the necessary amount of the drug can be known and applied with exactness. The effect of the drug on the accommodation can be watched from the time of appli-

1. Stille: Therapeutics and Materia Medica, Philadelphia, Blanchard & Lea 1860, vol. 1, p. 759.

2. Wood, Casey A.: Improper Use in Medical Literature of Certain Words and Phrases, J. A. M. A. **24**:352 (March 9) 1895.

3. Donders, F. C.: Accommodation and Refraction of the Eye, London, New Sydenham Society, 1864, p. 584.

4. Norris: Tr. Am. Ophth. Soc. **4**:369, 1886.

5. Risley: Tr. Am. Ophth. Soc. **3**:228, 1881.

6. Derby, H.: Tr. Am. Ophth. Soc. **2**:139, 1874.

cation to the time of maximum effect and of complete recovery. Physicians who use a cycloplegic for diagnostic purposes should understand what it does and be able to limit to a minimum the discomfort, disabilities and inconveniences that it causes. However, the exact effects of known amounts of the alkaloids deserve to be studied more carefully.

Cycloplegia is closely associated with mydriasis. All of the drugs which act as cycloplegics are also mydriatics. This fact must be taken into consideration in all of the diagnostic uses of cycloplegia. The eye is used with its pupil contracted by outdoor light for distant vision or by convergence for near vision. Its refraction under cycloplegia is measured with a dilated pupil. The differences in ocular refraction between the contracted and the dilated pupil should be recognized in all diagnostic uses of cycloplegia. Cycloplegia is necessary in order to learn the refractive condition of the eye at rest and to prescribe the glasses that can be used with the maximum of rest and the minimum of exertion for the eyes. This is extremely important for eyes that are to be used most of the time for near vision. But such measurements of refraction can be made only when one understands the changed refraction of the dilated pupil. Problems of aperture are considered in the preliminary planning and construction of optical instruments. In the eye these problems depend on the varying size of the pupil, but should be considered.

A pupil with a diameter of 4 mm. generally has a regular and equal refraction throughout its area. Even if it presents regular astigmatism, the astigmatism is the same in different parts, so that a spherocylindric lens will give a complete correction of the ametropia. When the pupil is fully dilated, however, as it is by any of the cycloplegic drugs, the peripheral parts of the pupil show errors of refraction which are different from any in the central zone and which often differ from one another.

The central zone is called the visual zone.[7] It admits the light by which one sees in outdoor daylight or when details are to be distinguished by near vision. The dilated pupil of 8 mm. admits four times as much light as that of 4 mm. With the dilated pupil, three fourths of the light comes through the peripheral zone and is not focused as in the visual zone or by the glass that corrects the visual zone. Nevertheless, the lenses chosen when the pupil is dilated may be those that correct the visual zone. No part of the peripheral zone focuses the light passing through it well enough to form an image that can compete with that formed by the visual zone. Sometimes, however, the peripheral refraction considerably affects the choice of

7. Jackson: Tr. Sect. Ophth., A. M. A., 1894, p. 75.

lenses with the dilated pupil. This is particularly likely to occur when some part of the peripheral zone has a decided, regular astigmatism, the meridians of which may not conform to those of the visual zone. In such cases the axis of the cylinder, chosen at a postcycloplegic test, may vary from that chosen when the pupil was dilated. The skiascopic examination, which compares the movement of light and shadow in the different parts of the pupil, will best explain such disagreements. The visual zone, however, must be used when the eye is doing its ordinary work. This zone is the part of the pupil that must be optically corrected to save the patient from eyestrain; hence, the importance of the postmydriatic tests.

Cycloplegia is commonly necessary to find the amount of hyperopia or myopia up to middle age. But as it is always associated with mydriasis, it opens up the wide variety of refractive conditions present in most dilated pupils. Many of the apparent variations and contradications found in refraction under the influence of cycloplegia are due to the different errors of refraction actually present in the dilated pupil, and not to faulty cycloplegia. The first papers on retinoscopy, published in French by Mengin [8] and Parent [9] and in English by Forbes [10] and Charnley,[11] contained allusions to different forms of light and shadow seen moving in the pupil. But the significance of the shapes was not explained until later. Bowman's somewhat linear shadow of regular astigmatism and the revolving triangles of shadow or light in the pupil due to conical cornea were not clearly explained when first reported.[12] Lindner's [13] skiascopy with cylinders is not yet fully appreciated as a means of studying the irregular astigmatism which remains after regular astigmatism has been corrected.

The unrecognized variations in the refraction of different parts of the dilated pupil have done much to cause confusion as to the comparative strength of the different cycloplegics and to perpetuate and mask the glaring defects and consequent unreliability of common methods of using cycloplegics. Donders [3] chose atropine sulphate as the best cycloplegic; he found that 1 drop of a solution of 1 part of drug to 120 parts of water could be relied on to produce cycloplegia, but he also found that in the dog, one millionth grain applied to the iris would perceptibly dilate the pupil. The human iris is equally sen-

8. Mengin: Rec. d'opht. **5**:122, 1878.
9. Parent: Rec. d'opht. **2**:65 and 87, 1880.
10. Forbes: Roy. London Ophth. Hosp. Rep. **10**:62, 1880.
11. Charnley: Roy. London Ophth. Hosp. Rep. **10**:344, 1882.
12. Donders,[3] p. 490.
13. Lindner: Die Bestimmung des Astigmatismus durch die Schattenprobe mit Cylindergläsern, Berlin, S. Karger, 1927.

sitive to mydriatics. Murrell [14] found that repeated instillations of a 0.1 per cent solution of scopolamine hydrobromide produced cycloplegia. Every newly discovered cycloplegic has been brought forward with the claim that its different action makes it better than its predecessors. Discussion has been aroused, and observations have been recorded. Marlow [15] used one or two instillations of a 0.2 per cent solution of scopolamine hydrobromide. Few comparative tests have been made of the relative strengths of different cycloplegics since it was reported that these are: homatropine, 1; atropine, 30, and hyoscyamine, 75.[16] It has been generally accepted that atropine should be prescribed in a 1 per cent solution, and duboisine, hyoscine and scopolamine hydrobromide in about one-half that strength. Little has been published, however, that tends to render the knowledge of the subject more exact.

Most of the uncertainty about cycloplegics, however, has arisen from the indefinite and inefficient method by which the drugs have been applied to the eyes when resorted to for the diagnosis of errors of refraction. If the pupil was dilated, it was assumed that the drug had been applied properly, although useful cycloplegia requires a ten times more powerful drug than is needed to produce complete mydriasis. In order to affect the size of the pupil or the state of accommodation, the drug must act on the nerve endings in the sphincter of the iris and in the ciliary muscle. To accomplish this by local application of the drugs, they must be placed on the cornea in sufficient amount and strength of solution to diffuse from without inward through the cornea and the aqueous humor. The part of the drug which passes through the conjunctiva does not reach the aqueous humor and the intra-ocular muscles except as it is taken up by the veins and enters the general blood stream. If cycloplegics are applied in a manner proper to solutions employed in disease of the conjunctiva, little effect will be produced on the ciliary muscle.

A cycloplegic should be dropped on the upper edge of the cornea and allowed to spread over the entire corneal surface before it is wiped away by the lid or diluted with the fluid contents of the conjunctival sac. Applied in this way, it will produce more than twice as much effect on the iris and the ciliary muscle as will the same amount merely dropped into the conjunctival sac. To get full cycloplegia with the least general toxic effect, the application of the drops to the cornea must be repeated. This was realized with reference to the use of homatropine forty years ago. But it has not been sufficiently noticed or emphasized

14. Murrell: Ann. Ophth. & Otol. **4**:478, 1895.
15. Marlow: Ophth. Rev. **30**:74, 1911.
16. Jackson: Tr. Sect. Ophth., A. M. A., 1895, p. 21.

in standard textbooks to teach its general observance and importance. The recent "Clinical Physiology of the Eye" of Adler [17] explains the permeability of the cornea by fluids and salts. Its impermeability to colloids, Duke-Elder [18] pointed out, is essential to keep it optically homogeneous. In his "A Treatise on Diseases of the Eye," Weeks [19] gives a table of data regarding cycloplegics; he adds: "The writer is accustomed to use cycloplegics and mydriatics for refraction work at the office, under his direct supervision. If for any reason the cycloplegic is prescribed for use at the patient's home, explicit directions are given."

So little attention has been given by authors and teachers to details regarding cycloplegia that many ophthalmologists ignore the methods of making it effective and leave the applications of drugs to untrained assistants or members of the patient's family who are ignorant of the necessary details of the use of cycloplegics. The drugs are sometimes applied in disks of gelatin placed above and slightly outward from the corneal limbus. The drug is thus effectively applied to the cornea. Homatropine used in this way, with an admixture of cocaine, was found to be an effective cycloplegic. Wood [20] ranked it the best for efficiency and quick recovery.

Inefficient methods of placing the drugs in the eye are responsible for much of the uncertainty regarding the use of cycloplegics. When they are properly used, cycloplegics are as constant and as reliable in their effects as any drugs known to medicine. If a child comes to the physician after an instillation of a 1 per cent solution of atropine sulphate, three times a day at home, and shows a scarcely perceptible enlargement of one pupil, he has received utterly ineffective medication; but when 1 drop of the same solution, properly placed on the cornea, produces complete cycloplegia within one hour, the fault is demonstated to be not in the solution but in the manner of application. This shows the utter unreliability of cycloplegics used without direct supervision or explicit instructions.

Statements concerning the efficiency of single drops of cycloplegics do not hold for inefficient applications, even when the drops are repeated for days or weeks. The application of a cycloplegic demands the care and skill of the trained ophthalmologist just as much as anything else he does for his patient.

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17. Adler, F. H.: Clinical Physiology of the Eye, New York, The Macmillan Company, 1932, p. 20.

18. Duke-Elder, W. S.: Text Book of Ophthalmology, London, Henry Kimpton, vol. 1, p. 423.

19. Weeks, J. E.: A Treatise on Diseases of the Eye, Philadelphia, Lea & Febiger, 1910, p. 682.

20. Wood: Ophthalmic Therapeutics, Chicago, Cleveland Press, 1909, p. 61.

Two things retard greatly the understanding of ametropia and its effects, which can be removed by correcting glasses: failure to recognize the symmetrical and irregular aberrations of the dilated pupil, and lack of exact knowledge as to the effects of cycloplegics and the reactions and results that follow their application.

For hundreds of years, it was regarded as the chief duty of the physician to feel the pulse. What is known as blood pressure and of many mutations of other vital conditions gradually developed from this practice. It was Pasteur's study of crystals of tartaric acid, differences in yeast cells of different beers, souring of milk and the cause of disease in silk worms that brought about the greatest revolution in the knowledge of pathology. He who watches the reaction of a child or an adult when a cycloplegic is placed in his eye will obtain an understanding of the patient and of the connection of eyestrain with nerve disorders that he can never get from dictating prescriptions based on routine examinations by assistants.

A better knowledge of the action of cycloplegics will probably lead to changes in the choice of the drug used and in the method of using it. All of the experiments with cycloplegics show that large doses give a prolonged period of maximum effect. After the application of the drug, there is a period of rapid increase in the mydriasis and the cycloplegia. Then there is a period of complete cycloplegia and maximum dilatation of the pupil which may last for several days; after that there is a period of gradual recovery. When small doses are used, there is no noticeable period of maximum effect. The effect gradually increases until the maximum is reached and then gradually declines until recovery is complete. For therapeutic rest, a period of maximum effect may be useful, but for diagnostic purposes it may only add to the discomfort and inconvenience of cycloplegia. The maximum should continue long enough for the necessary repetition of tests. But unnecessary prolongation of the period will make the patient reluctant to submit to the cycloplegic.

When there is uncertainty about the completeness of the cycloplegia, repeated instillation to make sure that it will be effective is a natural precaution. However, with the good method of testing the completeness of the cycloplegia which one has in skiascopy with correcting glasses, one is not justified in submitting the patient to unnecessary inconvenience or to the risk of toxic symptoms.

Probably the gradually increased effect on the iris and the ciliary muscle and the gradual decrease depend on changes in the amount of the cycloplegic in the aqueous humor. When the cycloplegic rises above a certain amount, no further effect can be produced, and the effect will not be reduced until the amount of drug falls below that level. Experiment can determine the minimum strength or the minimum number of instillations that can be expected to produce complete cyclo-

plegia. When the shadow test shows that cycloplegia is complete, the amount of ametropia is established. One is therefore justified, after careful investigation, in omitting the large and repeated doses of cycloplegics which are sometimes used to make complete cycloplegia certain. By repeated instillations it is possible to use cycloplegics with certainty of efficacy in solutions weaker than those previously employed. Instead of a 1 per cent solution of atropine and a 0.5 per cent solution of scopolamine hydrobromide, complete cycloplegia can be secured with two or three instillations of solutions of one tenth or even one-twentieth these strengths. Experiments made by Davis [21] seemed to prove that these weaker solutions are entirely practicable. The discovery and use of homatropine seem to indicate an advance toward the ideal method for the use of cycloplegics. Davis has found a striking similarity in the curves for effects secured with homatropine and those secured with weaker solutions of atropine and scopolamine hydrobromide.

Oculists who use more than one of the cycloplegics commonly state an age after or before which a certain cycloplegic should be used, such as the use of atropine in young children and homatropine in adults after 30. The reason for this is the assumption that the accommodation is stronger and harder to overcome in early life. The subject of variations due to age in the action of any particular cycloplegic, however, has had little investigation. It deserves to be carefully studied. Exact, definite facts in this regard may be of practical importance with reference to the choice of a cycloplegic, and it may throw some light on the mechanism of accommodation.

That Donders named his book "Accommodation and Refraction" may show a foreknowledge of the importance of the function of accommodation, which he brought to the attention of the medical profession. The thirty years that followed the publication of his book saw the development of partisan discussions and opposing schools of thought. One side urged that cycloplegia is an important therapeutic measure, and that up to an indefinite middle age, it is necessary to the prescription of glasses. The other held that cycloplegia should rarely be used, and that it is scarcely ever necessary. With increased resources in the methods of diagnosis, it now seems possible to avoid the undesirable effects of cycloplegia and to give it a wider, more exact and more efficient application.

Skiascopy affords an understanding of the irregular aberrations of refraction in the periphery of the pupil which are made important by mydriasis. It presents a reliable method of determining when cycloplegia is complete. This has rendered unnecessary the use of excessive amounts of cycloplegics and has made cycloplegia much less alarming

21. Davis, L. L.: Unpublished thesis, 1933.

and formidable to the patient. The cross-cylinder has made it possible to detect and measure changes in astigmatism; thus frequent repetitions of cycloplegia are less often necessary.

With an increase in the number of drugs serviceable in producing cycloplegia, and with varied methods of applying them, the certainty of complete relaxation of the ciliary muscle is made available for a larger proportion of cases of refraction. These advances, however, like other advances in modern medicine, are available only through the study, watchfulness and judgment of educated physicians.

Diagnostic cycloplegia is practicable through the peculiar permeability of the cornea to fluids and crystalloids. By placing drops of a cycloplegic solution of known efficiency on the cornea and keeping them there for the necessary time, cycloplegia can be attained, rendered complete and maintained as long as necessary; it can then be overcome or can be permitted to pass off with the least annoyance or inconvenience to the patient. Cycloplegia adds great certainty to the diagnosis of refractive errors of the eye and should be understood and employed by every one who is engaged in ophthalmic practice.

XANTHOMATOSIS OF THE ORBIT

REPORT OF TWO CASES

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There is a tumor of the orbit arising from the frontal bone which has the following characteristics: (1) formation of the tumor below the upper bony margin of the orbit causing exophthalmos; (2) a lesion of the frontal bone showing as a defect of the bone in the roentgenograms, not connected with the nasal sinuses; (3) certain histologic peculiarities; (4) slow growth; (5) benignancy, cured by operation, with no tendency to recurrence and no influence on the patient's health. The two following cases illustrate this condition.

REPORT OF CASES

CASE 1.—*History.*—M. S., a man, aged 43, came to the Herman Knapp Memorial Eye Hospital on Dec. 6, 1932, complaining that the left eye had protruded and that the vision in that eye had been failing for three months. There were no headache or nasal discharge and no general symptoms. A firm mass like bone could be felt in the upper part of the left orbit continuous with the frontal bone. The vision of the left eye with a correcting lens was 10/200. The periphery of the visual field was normal; the blindspot was enlarged, and there was a central scotoma. Examination of the fundus revealed optic neuritis, and the retina at the posterior pole was corrugated in the form of parallel folds which ran from down and in to up and out. The eye was pushed forward and downward, and its motility upward was restricted. The right eye was normal.

In the roentgenogram a rarefaction of the roof of the left orbit was noticeable with absence of the bony margin, and the external boundary could not be delineated. The contour of the frontal sinus was intact (fig. 1). This cleared area suggested a lesion of the bone in the upper and outer wall of the orbit not connected with the sinuses. Examination of the nose gave negative results. As the exact nature of the process was uncertain, an exploratory operation was decided on.

Operation (Dec. 13, 1932).—A curvilinear incision was made below the left eyebrow exposing a bony structure which extended downward from the outer half of the superior wall of the orbit and was adherent to the soft tissue below. The bone was chiseled away; it proved to be a very thin layer covering a thickened soft membrane of a golden brownish hue. This membrane was incised, and a cavity was exposed which contained a quantity of thin, watery fluid with many glistening yellow scales. The cavity extended deep into the orbit, and its walls involved the lower bony plate of the frontal bone well into the external frontal process. The underlying medulla of the bone was red, granular and uneven, but the dura was nowhere exposed and there was no communication with a nasal sinus. The walls were curetted and the bony edges smoothed off; the external wound was sutured. Prompt healing followed, and on December 29, the vision had improved to 20/70. The optic nerve showed neuritic atrophy. The oblique lines in the eyeground were unchanged. These lines were like bands, lighter than the usual

color of the fundus, presumably situated in the choroid; the folds were not solely in the retina as the vessels did not dip down as they do in retinal separation, so that the condition suggested inflammatory changes in the sclera. The contents of the cyst consisted of red cells, polymorphonuclear leukocytes and many cholesterol crystals.

The microscopic examination of the tumor wall presented a connective tissue framework with many fissures from cholesterol crystals surrounded by giant cell proliferation.

A general physical examination gave negative results except for slightly sclerotic radial arteries and a barely palpable liver. The laboratory examination showed normal blood sugar during fasting and a normal sugar tolerance curve following the ingestion of 100 Gm. of dextrose by mouth. The blood sugar was

Fig. 1.—Roentgen appearance in case 1.

109 mg. per hundred cubic centimeters; the urea nitrogen, 18.70 mg.; the serum albumin, 5.14 mg.; the serum globulin, 2.59 mg., and the cholesterol, 300 mg. The Wassermann reaction of the blood was negative. The urine was normal. The basal metabolic rate was 5 plus.

On September 29, vision in the left eye with -1 sph. $+4$ cyl., axis $45° =$ 20/40. The visual field was normal. There was no deformity or diplopia; the left eye was in its normal place.

CASE 2.—*History.*—A. L., a man, aged 28, seen on Dec. 23, 1914, stated that the right upper lid had felt full and swollen for five years, and that the right eye had been protruding for two years. The right eye was pushed down and forward; the vision in that eye was 20/50; the field and fundus were normal. There was a mass to be felt within the upper border of the orbit, bony in texture and continuous with the frontal bone. At the inner side of the orbit this mass became soft and extended deep into the depth of the orbit. A roentgenogram was not taken. The movements of the eye were unrestricted. The nose was normal.

The left eye was normal. As the Wassermann test proved to be 4 plus, the patient was given intensive treatment for several months. There was no change in his orbital condition, and an operation was then decided on.

Operation (Sept. 30, 1915).—The usual curvilinear incision was made below the eyebrow, exposing the margin of the right orbit. A thin, bony wall was uncovered, and an irregular, lobular soft tumor presented within the upper wall of the orbit directly continuous with the bone. The mass was incised and a cavity exposed which was filled with soft, gritty, broken-down material. This cavity extended deep into the orbit and was adherent to the orbital periosteum below. Above there was a large defect in the outer plate of the bone, and at one point the tumor process had perforated the bone and was adherent to the dura. Anteriorly and externally, the orbital layer of the bone was absent and the medulla of the bone was red and roughened. The tumor was removed as thoroughly as possible; the walls were curetted, and the bony edges smoothed over. The external wound was sutured. Healing was uneventful.

The patient was seen again in May, 1932, nearly seventeen years later. His general health had been good until recent years and he was now undergoing treatment at the Presbyterian Hospital for general and coronary arteriosclerosis. This length of time (seventeen years) without any recurrence or development of lesions in other parts of the body showed that the process was benign. The vision in the right eye was 20/20; there was no sign in the orbit of any recurrence, and no deformity could be observed, though a small defect in the upper orbital margin appeared in the roentgenogram.

The microscopic specimens of these tumors were similar and proved to be examples of the same process. Dr. James Ewing examined the sections and wrote out the following report:

"The main histologic feature in both of these cases is the presence of many elongated rhomboid crystal beds about which many foreign body giant cells have formed, and between which there is moderate proliferation of various indifferent tissue cells. These areas make up the larger portions of the tumor. In other portions there are small cysts formed by liquefaction of proliferating cells which contain lipoid material. These cysts are not unlike those seen in atheroma of the aorta. About the cysts and in many other foci there are typical xanthoma cells, single and in sheaths. The course of changes in this process is rather clear. It begins with lipoid deposits in the xanthoma cells, proceeds to the formation of cysts by liquefaction in some places and to the separation of rhomboid crystals with formation of giant cells in other places. That the process begins in the bone marrow is indicated by the presence of many bone trabeculae surrounded by the degenerating lipoid cells. At no point is there any trace of epithelium found such as is present in true cholesteatoma of epidermal origin. The process is essentially that of xanthomatosis of the type observed in Schüller's disease."

Rowland [1] has given the name xanthomatosis to certain manifestations of lipoid metabolism with storage tumors of lipoid material appearing in various places. This disturbance of lipoid metabolism

1. Rowland, R. S.: Xanthomatosis and Reticulo-Endothelial System: Correlation of Unidentified Group of Cases Described as Defects in Membranous Bones, Exophthalmos and Diabetes Insipidus (Christian's Syndrome), Arch. Int. Med. **42**:611 (Nov.) 1928.

or of lipoid excretion may cause changes which are widespread, as Chiari [2] suggested, or circumscribed in the form of granulomatous deposits as occur in Schüller-Christian's disease and in the cutaneous xanthomas. The microscopic examination shows the process to be not a neoplasm but the result of the phagocytic action of the reticulo-endothelial system which stores an excess of lipoids and produces hyperplastic new formations, i. e., lipoid storage tumors. The xanthoma cell is a cell of reticulo-endothelial origin infiltrated with lipoids, and

Fig. 2.—Early stage of process showing xanthoma cells and crystal beds.

lesions of xanthoma are the hyperplastic reaction of the reticulo-endothelial system resulting from the infiltration of lipoids in excess of the body fluids. A localization of this process produces the hyperplastic nodular lesions. First, xanthoma cells are present, then in older nodules connective tissue predominates; the fatty substance may appear as fine granules or as crystals in rods or in clusters; red blood cells and iron pigment are also present.

2. Chiari, H.: Die generalisierte Xanthomatose vom Typus Schüller-Christian, Ergebn. d. allg. Path. u. path. Anat. **24**:396, 1931.

Fig. 3.—High power photomicrograph of advance process showing giant cells forming about crystals.

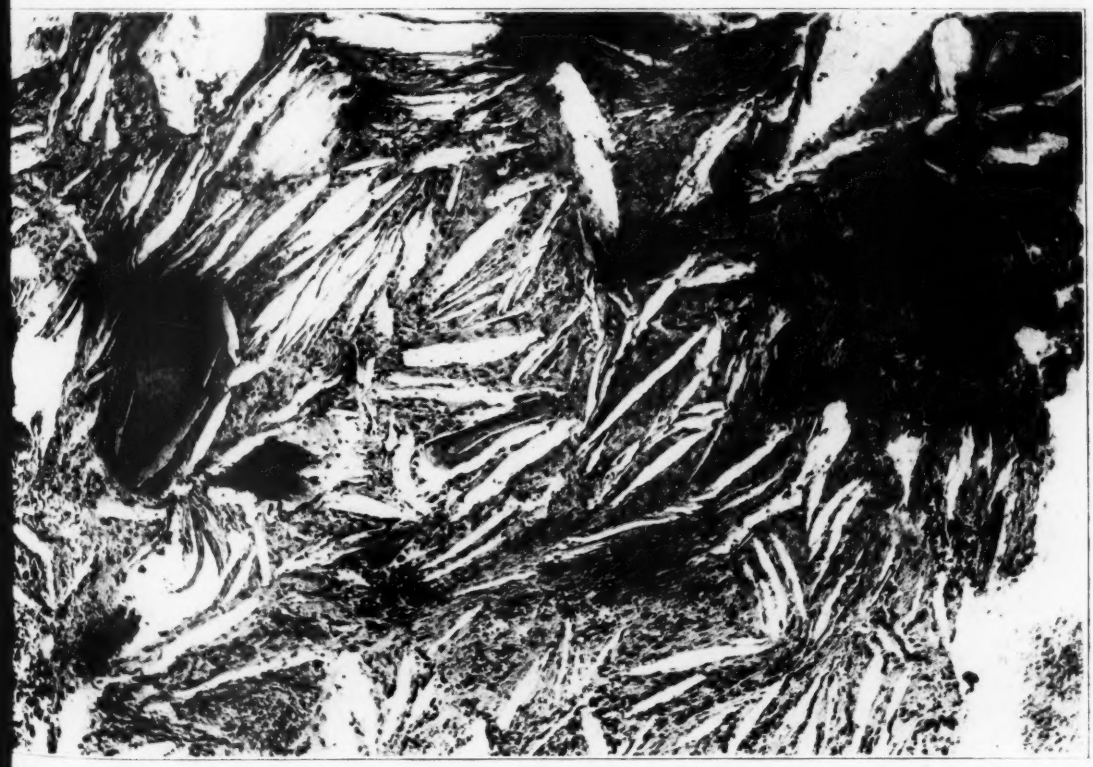

Fig. 4.—Section of bone tissue showing that the process affects the bone primarily.

Aschoff [3] said that with increasing cholesterol in the blood a storage takes place in the reticulo-endothelial cells in which the cholesterol is dissolved out and stored. Connective tissue proliferation then results. One may assume the presence of hypercholesteremia and tissue change turned for lipoid storage. The Schüller-Christian disease occurs only in young children and involves the bones of the skull with diabetes insipidus and exophthalmos. A roentgenogram of the skull in Schüller-Christian's disease is similar to that found in the two cases reported except that the lesions are more generalized. The predilection for the orbit is interesting, and in the Schüller-Christian disease is due to a lesion of the ethmoid and small wing of the sphenoid.

Two cases occurring in adults were reported by Chester [4] as a variant of the Schüller-Christian syndrome, in which lipoid granulomas were found in the long bones, and there was diffuse involvement of the heart.

Sosman,[5] in an excellent review of the subject with reports of two new cases, called attention to the value of roentgen treatment and to the fact that frequently no other treatment is available.

No cases of xanthomatosis of the orbit have been recorded in the literature. Xanthomatosis as affecting the eyeball has been repeatedly described in ophthalmic literature, and a complete description by Heath [6] appeared recently in the ARCHIVES. The nearest approach to this condition can be found in a group of unusual tumors of the orbit which have been described as cholesteatoma. Birch-Hirschfeld [7] spoke of the unusual cases of cholesteatoma of the orbit which are allied to the dermoids, but differ in not having a defined wall and are situated subperiosteally. They consist in stearin-like masses and polygonal scales like epidermal scales packed together in lamellae. A few case reports are quoted, but the descriptions are not clear and the correctness of the term cholesteatoma is not proved, especially as pathologists seem to be abandoning the belief that cholesteatoma is a definite form of tumor.

According to Aschoff, in the so-called cholesteatoma (mother-of-pearl) tumor, the mucous membrane becomes epidermis, the keratinized

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3. Aschoff, Ludwig: Pathologische Anatomie, ed. 6, Jena, Gustav Fischer, 1923, p. 395.

4. Chester, W.: Ueber Lipoid Granulomatose, Virchows Arch. f. path. Anat. **279**:561, 1930.

5. Sosman, M. C.: Xanthomatosis (Schüller-Christian's Disease; Lipoid Histiocytosis), J. A. M. A. **98**:110 (Jan. 9) 1932.

6. Heath, Parker: Ocular Lipoid Histiocytosis and Allied Phenomena, Arch. Ophth. **10**:342 (Sept.) 1933.

7. Birch-Hirschfeld, in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, Wilhelm Englemann, 1930, vol. 9, p. 566.

epithelial cells form layers of mother-of-pearl-like glistening scales, and tumors result which contain cholesterol. The center may soften and fill with detritus. The growing cholesteatoma causes a smooth, globular pressure atrophy or erosion of the underlying bone.

The most recent article on cholesteatoma of the orbit is by Pinkus.[8] He reported on the two following cases: In case 1, the roentgenogram showed a clearing in the upper orbital margin. At operation the bone was found thinned; the tumor contained reddish-brown fluid with many glistening crystals, degenerated cells, detritus and cholesterol crystals. The microscopic appearance consisted in more or less degenerated cells with many cholesterol crystals. In case 2, the roentgenogram showed a clear area in the upper part of the right orbit. The contents were a brownish fluid with many crystals. Microscopically, the tumor presented a granulomatous cellular connective tissue with many crystals, giant cells and hemorrhagic products. In discussing these tumors, Pinkus spoke of the inadequacy of the term cholesteatoma and suggested the term pseudocholesteatoma of the orbit. Pinkus' cases presented the same roentgen changes in the frontal bone as were present in the ones described in this article. The findings at operation were also similar. Their histologic picture, which according to Pinkus[9] resembled that of the cases of so-called cholesteatoma of the orbit, in my opinion belong to xanthomatosis.

The two cases reported in this article can be regarded as a localized manifestation of a xanthomatous process occurring in the orbit without any other symptoms of this condition in the patient except a hypercholesteremia.

The predisposition for localization of this process in the orbit is interesting in view of the frequent involvement of the orbit in Schüller-Christian's disease and in the cases described here; possibly an explanation for this can be found in the fact that the frontal bone is so easily traumatized.

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8. Pinkus, H.: Klin. Monatsbl. f. Augenh. **90**:145, 1933.
9. Pinkus,[8] p. 151.

PREVENTION OF SPONTANEOUS RETINAL DETACHMENT

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Knowledge concerning the etiology of idiopathic detachment of the retina, also called spontaneous retinal detachment, has increased during the last few years to such an extent that it may be asked today whether it is possible to prevent the outbreak of the disease or at least to stop its progress after it has begun and thus assure a good prognosis for operation.

To explain these problems, one must first know how spontaneous retinal detachment originates. Then only may one discuss the prevention of this disease.

The significance of the retinal tear as the immediate cause of spontaneous retinal detachment can hardly be questioned. If one succeeds in closing the communication between the vitreous cavity and the subretinal space by any kind of operation, the detachment disappears entirely within a few days. Besides this clinical fact, experiments on models have shown that a displaceable retina with a flap-hole must become mechanically detached when the eye performs the normal movements. On account of the great importance of these experiments on models, I wish to discuss them briefly. It is possible to demonstrate on the model of an eye the mechanical forces which, on account of a flap-hole in the retina, cause detachment if the eye moves. A round glass flask is chosen as the simplest model. The model retina consists of a layer of pyroxylin (celloidin) containing enough aluminum powder to render it more visible and somewhat adherent. By this adhesion one gets a better proof of the detaching forces, and at the same time the self-detaching tendency of the model retina is counteracted.[1a] A hole is first made in the model retina in such a manner that the margin of the hole remains flat and does not protrude. Now, if the model is rotated around its center in a manner similar to the normal movements of the eye, nothing will happen. The model retina remains in place

1. Lindner, K.: (*a*) Ueber die Herstellung von Modellen zu Modellversuchen der Netzhautabhebung, Klin. Monatsbl. f. Augenh. **90**:289, 1933; (*b*) Ein Beitrag zur Entstehung und Behandlung der idiopathischen und der traumatischen Netzhautabhebung, Arch. f. Ophth. **127**:211, 1931; (*c*) ibid., p. 213; (*d*) Ueber die Verwendung der Lochbrille bei Behandlung von Netzhautabhebung, Ztschr. f. Augenh. **79**:191, 1932.

and well attached. But if the hole is made so that its margin protrudes, the layer of pyroxylin soon becomes detached (fig. 1). At first this detachment spreads slowly, but later with each movement it becomes more extensive.

The explanation is as follows: If the model is rotated back and forth around its center, the liquid inside the model, according to the law of inertia, will not follow immediately but will lag behind. If the model suddenly stops and moves back, the liquid first continues its former direction and then returns slowly in the opposite direction. Briefly, there is always a difference between the movement of the wall

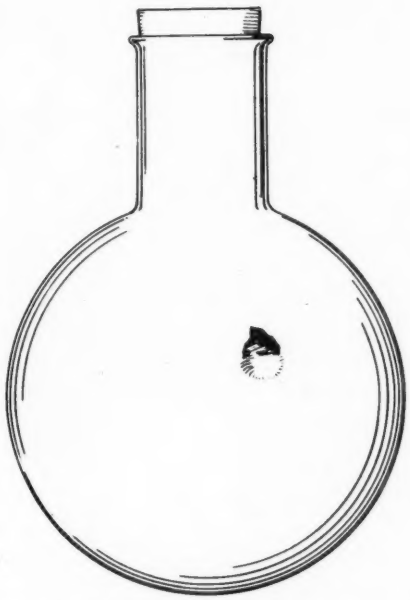

Fig. 1.—Model used to illustrate detachment of the retina. Rotation of the flask causes disconnection of the layer of pyroxylin (celloidin) after a hole with a protruding margin (retinal tear) has been made.

of the model and that of the liquid next to it. Thus the moving liquid strikes against the protruding margin of the hole, detaching the layer of pyroxylin. If some liquid gets under the layer, it acts according to the same law of intertia and detaches the retina more and more. But if the model is put at rest, the formerly detached retina, because of its normal texture, flattens out again and the detachment becomes shallow. The position of the model also has some influence on the flattening of the artificial detachment, because the membrane of the model is heavier than water, just as the retina is heavier than the vitreous. While the rotating movements of the model detach the retina more and more, there is, on the contrary, no detaching influence visible if the model is moved

forward and backward or up and down, without being rotated. In all movements of the model it is the rotating component only which influences the detachment.

It is not easy to prepare good working models. Too much aluminum powder renders the layer too adherent; too little powder causes no adhesion at all. Besides, a hot, dry atmosphere increases the tendency of the pyroxylin to shrink and to detach itself.

By this experiment it can be demonstrated that retinal detachment must take place in every case in which the retina shows a so-called flap-hole which, for certain reasons (to be explained later), always opens into subvitreous fluid or liquefied vitreous.

Clinical observation agrees to some extent with the results of this experiment in many cases. Immobilization of the eyeball may stop the

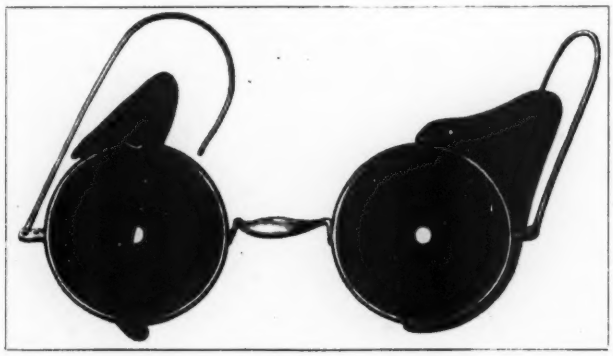

Fig. 2.—*Lochbrille* (hole-spectacles), used to prevent movements of the eye in cases of detachment of the retina.

progress of detachment and diminish its depth. Exceptionally, the retina may become totally reattached by immobilization alone. But as soon as immobilization is discontinued, the detachment reappears within a short time and spreads out again. By immobilization of the eyeball is meant the exclusion of movements of the eyeball in the orbit. For instance, walking without moving the head will have no influence on the detached retina. In order to inhibit ocular movements, I used the so-called *Lochbrille* (hole-spectacles) in my clinic as early as the spring of 1930. It is the simplest instrument for excluding movements of the eye [1b, d] (fig. 2).

But the conditions in most cases of detachment are not so simple. The eye, suffering from spontaneous detachment, is filled not with watery fluid and normal vitreous but, more or less, with a fluid behind the normal vitreous (subvitreous fluid) or with liquefied and partially solid vitreous. This solid vitreous mass, which is still connected with

the retina in its anterior region, takes an active part in the process of détachment. The influence of the solid vitreous complicates the mechanism of retinal detachment and its ophthalmoscopic appearance. This peculiar fact I shall explain before continuing:

The solid vitreous diminishes somewhat in volume in the neighborhood of a retinal tear with detachment. At present, clinical observation only gives evidence of this fact, for which there is no experimental foundation as yet. The smaller the degree of myopia, the less, as a rule, will be the amount of liquefaction or detachment of the vitreous, and the greater will be the amount of normal vitreous. When there is more solid vitreous present, one sees a quite different form of retinal detachment. In the latter case, the detached retina has a buckled appearance, giving the impression of an exudative process. This appearance was at

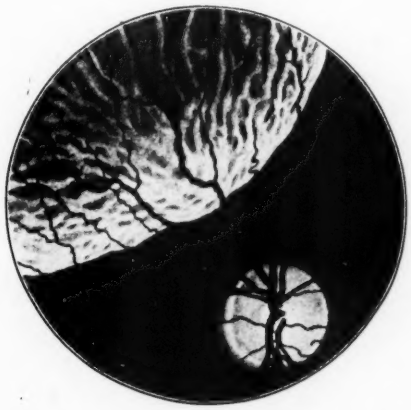

Fig. 3.—Appearance of the retina in detachment, showing buckling caused by adhesion to the solid vitreous.

one time the strongest argument for the exudative theory of retinal detachment. This buckled retina does not behave like the model retina in the experiment. It is not influenced by immobilization or by different positions of the eyeball. There is no floating movement of the detached retina visible when the eye moves. But sudden movements of the eye cause slight oscillations of the retina. This is due to the movements of the vitreous gel, which is intimately connected with the retina in its anterior parts and which communicates its oscillations to the retina. There is a definite sign of the connection of the retina with the vitreous: At first the surface of the buckled retina is not smooth, as it would be in the case of a simple exudation, but shows many fine wrinkles, proving that the retina is adherent to the shrunken vitreous gel (fig. 3).

After a period of from six to eight weeks or more the vitreous liquefies to a great extent and thus releases the retina. In cases of this

type, therefore, immobilization of the eye by the *Lochbrille,* with rest in bed, will at first not improve the condition at all. Sometimes it will not even prevent further spread, owing to the progressive contraction of the vitreous gel. Later, however, when the vitreous becomes liquefied to a certain extent, the detached retina will flatten out if the eye is immobilized.

I believe that in detachment there is a reversed stream of intra-ocular fluid which moves from the ciliary body toward and through the retinal hole and which is absorbed by the exposed choroid. This stream causes the neighboring vitreous first to diminish in volume and to draw the adherent retina with it into the interior of the eye in a buckled form. Later on, through the action of this stream of fluid, the vitreous becomes more and more liquefied. If, in an early stage of detachment, this abnormal stream is stopped by an operation, the vitreous may again return to its former volume. I consider this explanation as the most probable one for the behavior of the vitreous in cases of retinal detachment. That such a reversed stream of the intra-ocular fluid exists in retinal detachments—a theory which was at one time held by Leber in order to explain the lowered intra-ocular tension—has been proved in the case of the rabbit by the experiments of Lobeck and of Arruga.

If, therefore, one compares different cases of retinal detachments, one has always to take into account the condition of the vitreous. The more the vitreous is liquefied or detached the more the retinal detachment will behave like the model retina: The retina will float with each movement of the eye. Immobilization of the eyeball flattens the retinal detachment visibly. But if, in a particular case, the vitreous is slightly detached, or if only a small part of vitreous is liquefied and much normal vitreous is left, the active influence of the contracting vitreous becomes evident within the first weeks. One finds the peculiar buckled retina with fine wrinkles on its surface. This will not change with or without the use of the *Lochbrille* or with prolonged immobilization of the eye. If the eye moves suddenly during observation, the detached retina does not float but trembles slightly. After from six to eight weeks or longer, when the vitreous becomes more liquid, the area flattens out more and more, the fine wrinkles disappear and the retina becomes freely displaceable because most of the vitreous is liquefied. Then the *Lochbrille* produces a noticeable result, and different positions of the eye influence the form and distribution of the detachment. In cases of this type there is the best prognosis for operation. I have repeated these clinical observations and their probable explanation [1b, c] because they are indispensable for the understanding of the polymorphous behavior and the different appearances in cases of retinal detachment. I do not mention other complications which may occur, such as strands in the vitreous, the cohesion of adjoining retinal folds and other conditions.

Therefore, if clinical experience is considered in the light of mechanical experiments, the prevention of detachment must consist in the prevention of the retinal tear. If the vitreous is mostly liquefied or detached and shrunken into a small remnant behind the lens, the presence of the flap-hole alone is sufficient to cause detachment when the eye moves. But if there is a greater amount of solid vitreous left, the detachment is influenced by the beginning contraction of this vitreous. In most cases, influences of this kind are visible in the anterior part of the eye, never around the posterior pole, because the more solid vitreous always is situated in the anterior segment. In the posterior segment of the eyeball the vitreous is either liquefied or detached in nearly all cases of spontaneous retinal detachment. Otherwise, the contracting vitreous would detach itself in this place rather than draw the retina into the eye.

Is the formation of a retinal tear preventable? In observing different kinds of retinal tears, one often sees an eye with several tears, one of which must be the primary defect. Not all of them have the same origin and cause. First, I wish to discuss the formation of the most common retinal tear, the flap-hole of Gonin (1904). To answer the question of the origin of the flap-hole I shall consider the problem of retinal detachment with regard to the action of the vitreous when the eye moves.

According to clinical experience, spontaneous retinal detachment takes place only if the eye is predisposed to this disease. This predisposition is present in myopia, choroiditis and senility. These conditions often are combined; for instance, myopia may occur with senility or with choroiditis. All eyes with these conditions have one pathologic feature in common: partially detached or liquefied vitreous or both types. This is, in my opinion, the *conditio sine qua non* of any spontaneous retinal detachment.

In what way is partially liquefied vitreous or, still more often, partially detached vitreous the underlying condition of this disease? While in the model formerly described the action of a liquefied vitreous on the flap-hole was studied, a model with a normal vitreous must now be considered. Normal vitreous is not a liquid but a kind of gel. Therefore, a corresponding substance is chosen for the model; this is from 1 to 1.5 per cent white gelatin. A round glass flask of 500 cc. is filled with a hot solution of the gelatin, and this is allowed to coagulate at a low temperature. In hot weather the model has to be put in the ice-box. After the gelatin is well coagulated (after from eight to ten hours), the experiment is begun. The model is suddenly rotated, just as one would move one's eye, i. e., rotated and stopped suddenly. A moment later, a shock can be felt in the hand of the

operator. If the model is rotated back and forth in rapid succession, the operator may accidentally get a very strong shock. This experiment cannot be demonstrated at a scientific meeting, because the gelatin is soon broken up by the shocks. Therefore, the oculist must try this experiment himself. He will at once feel definitely the forces which, in my opinion, cause a flap-hole under certain conditions.

What is the explanation of this mechanical shock? The gelatin adheres to the glass wall. If the model is rotated, the neighboring gelatin, according to the law of inertia, will at first lag behind the movement of the glass wall. This is due, to a great extent, to the elasticity of the gelatin. But then the gelatin, by the same force of elasticity, jumps forward farther than the glass model itself, stopping suddenly at the limit of its elasticity and moving back again. This sudden stop of the whole mass of gelatin causes the shock which one feels in the hand. The same model, when filled with liquid, does not cause a shock, because the liquid moves freely without an obstacle, not being attached to the glass wall.

This fundamental experiment explains the cause of the formation of the so-called flap-hole. In a normal eye the vitreous adheres all around —very slightly to the retina of the posterior segment, a little stronger on the optic nerve and still stronger the nearer it is to the ora serrata. When the eye moves, the vitreous exerts a steady pull of varying intensity on these fastenings. In a normal eye these forces act uniformly and therefore at no particular place in a stronger or an isolated manner. But if the vitreous mass is detached from the posterior segment of the eyeball, or if it is irregularly liquefied, the shocks caused by sudden movements of the eyeball may at times exert a stronger pull on the parts of the retina to which the remaining vitreous mass is fixed.

For example, in a case in which the vitreous is detached from the posterior segment of the eye, if the line of adhesion of the vitreous is irregular, forming an isolated process toward the optic nerve, the force of pulling will concentrate first at this point (fig. 4). After a while the firmness of the structure of the retina is reduced here by repeated shocks, so that it finally tears. The forces of the swinging vitreous may be increased by two movements following each other rapidly in opposite directions, so that at these isolated places of adherent vitreous the retina will be doubly stretched. Strong and sudden movements of the eye occur, especially when the patient suffers an accident and involuntarily tries by sudden movements to protect his eyes.

There will be a similar effect if the vitreous is liquefied in an irregular way so that a mass of solid vitreous is left adherent to some portions of the retina in the anterior segment. In cases of this kind the mechanical conditions are not so easily demonstrated.

These experiments on models explain the sudden formation of large flap-holes, which can occur only as the result of a strong and sudden force acting from within the eye. Occasionally ruptures of vessels are observed with the formation of these flap-holes, giving evidence of the acting forces. Several cases are on record in which a typical flap-hole tear, with rupture of a crossing vessel, developed without detachment of the retina, or in which the flap-hole was confined to the inner layers of the retina only. Apparently the retina had grown together with the pigmentary layer and the choroid, and because of this pecular condition no detachment took place. So it is apparent that certain movements of the eyeball are the immediate cause of the formation of a typical flap-hole. At the same time, such a flap-hole tear always opens into a sub-vitreous liquid or liquefied vitreous, and the flap still connected with the solid vitreous hangs into the eye toward the anterior segment.

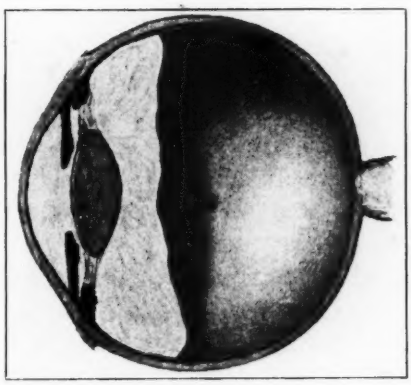

Fig. 4.—Retinal detachment in which vitreous is separated from the posterior segment of the eye. Because of the irregular line of adhesion, sudden movements of the eyeball exert uneven pulls on the remaining vitreous which may cause tears in the retina.

The next question is whether the vitreous, in detaching or liquefying from behind, may leave an irregular line of adhesion or whether this condition is due, as a rule, to other pathologic conditions.

The former theory, which was advanced by Leber, was based on the assumption that vitreous detachment precedes spontaneous retinal detachment in each case. Leber thought that the vitreous becomes detached and shrinks on account of some form of chronic peripheral choroiditis. After a certain period of straining of the retina this shrinking causes the retinal rupture. Gonin modified Leber's theory. According to him, detachment of the vitreous also develops at the posterior pole, owing chiefly to myopia. But the vitreous remains fastened to the retina more intimately in one place than in others as the result of previous choroiditis. The weight of the heavier vitreous and the move-

ments of the eye cause the retina to rupture at this point, forming the typical flap-hole, or an isolated piece of retina may be torn out.

Gonin thought that local choroiditis is necessary to fasten the detaching vitreous mass to the retina at some place in order to cause a more isolated adhesion and thus produce the flap-hole tear. As a rule, I have not seen choroiditic areas around flap-holes. Although it may be that some inflammatory processes in the choroid and retina which cause vitreous adhesions are not visible ophthalmoscopically, I believe that the normal adhesion of vitreous in the anterior region of the retina is strong enough to rupture a degenerated retina. The prevalence of the location of the typical flap-hole in the upper and outer quadrant does not speak for choroiditis as a local cause.

But not every primary hole is a flap-hole. Sometimes in the retina one observes a hole the corresponding piece of which floats in the vitreous. The piece must have been torn out at the place where there was a round isolated area of fixation between the retina and the vitreous mass, as Gonin pointed out many years ago. Vogt recently stated this again. Retinochoroiditis is the most probable cause of these adhesions. At any rate, tears of this nature are to be put in the same classification as the typical flap-holes, being caused by shocks of moving vitreous.

Hanssen demonstrated that holes may also develop as a result of retinal degeneration. But holes due to degeneration have no protruding margin. So it must be presumed that in these cases, too, the pulling action of isolated vitreous masses starts the detachment. The action of the contracting vitreous results not merely from the presence of a hole in the retina but only when the absorbing subretinal space is opened and starts the reversed stream of fluid toward the hole. Then only, through the influence of this reversed stream, does the vitreous begin to contract. Briefly, in regard to holes due to degeneration, movements of the eye must start the process of detachment and make the tear effective in bringing about the contracting action of the vitreous mass. In this way the detachment starts first around the hole, and the movement of the eye continues to increase it.

The so-called secondary holes have nothing to do with the problem. They develop during the further process of the spreading of detachments in places where the retina is fixed to the pigmentary layer and the choroid by some local pathologic process. For instance, holes in the macular region, in cases of spontaneous retinal detachment, nearly always are secondary ones. The model shows this process nicely. If the model is rotated, the forces developed by a greater amount of subretinal liquid in the progress of the detachment are so powerful that the layer of the model may rupture in several places where the membrane is too strongly fixed on the glass wall. Therefore, secondary holes also are prevented by immobilization of the eyeball.

To come back to the principle question of how the formation of a flap-hole or of a hole caused by the tearing out of a piece of retina can be prevented, there can be no doubt but that immobilization of the eyeball would prevent the formation of such holes. Holes caused by retinal degeneration cannot be prevented, but one is able to prevent the beginning of a detachment in cases of this kind by immobilization alone.

What means of immobilization of an eyeball are available?

1. One might interrupt the nerves of the ocular muscles after their entrance into the orbit. This would be the most effective and lasting way of immobilization. But, besides the difficulty of performing this operation, there would be some disagreeable consequences: ptosis and paralysis of the sphincter oculi and of the muscles of accommodation. Hence I do not think that this is advisable.

2. One might section all of the muscles of the eye in two sittings, excising each time a piece of muscle or tendon. The two obliques and

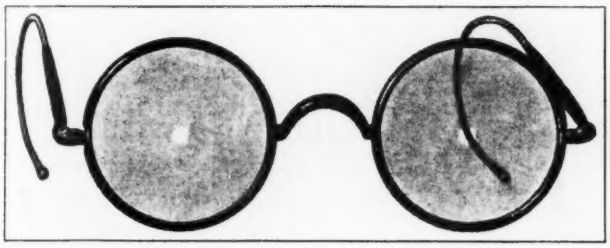

Fig. 5.—Glasses used by the author to inhibit ocular movements in cases of detachment of the retina.

the two recti might be resected in one sitting and the remaining two recti some time later. The eye will not become totally immobilized by these operations. Some mobility will remain, but great excursions will no longer be possible. Since a high percentage of cases of retinal detachment are now curable, I doubt whether patients would submit to this prophylactic procedure, even if they had already lost an eye from detachment. This procedure of immobilization may be recommended, however, as a curative measure in certain cases of inoperable monocular detachments.

3. In most cases I think that a simpler method would do as well: restriction of ocular eye movements by optical aid and by education regarding voluntary immobility of the eyes. While Punktal lenses are prescribed, when possible, in cases of ordinary refraction, the opposite method is used in cases of detachment of the retina: The glasses should prevent the patient from looking around. Therefore, glasses with strong peripheral aberration must be prescribed. For myopia requiring a lens of 10 diopters or more I prescribe Punktal lenses, but insert them into

the frame with the surface reversed. Of course, these glasses must correct the refractive error fully, so that there is no possibility of improving vision by looking through them obliquely. In milder cases of myopia there should be a surface of minus 10 directed away from the eye, and the other surface, directed toward the eye, should contain the necessary plus complement of refractive power. This helps the patient to keep his gaze constantly straight ahead. But he has to get used to these glasses, which are at first very disagreeable to wear. Besides, there is a slight cosmetic disadvantage, as the spectacles are somewhat conspicuous. Naturally, these glasses can never prevent involuntary sudden movements which may happen on occasions of sudden trauma. But if the daily movements of the eye are restricted the retina would resist an occasional shock, because its structure has not previously been altered by the daily shocks of the vitreous mass. I have prescribed these glasses in several cases of monocular involvement in which the other eye was blind from detachment. It remains to be seen whether detachment develops in the second eye in spite of this prophylaxis.

4. A safe way to immobilize an eye would be the use of the *Lochbrille,* which, by long use educates the patient to some extent to keep his eyes immobile, even if he discards the device later on. The *Lochbrille* may be prescribed without being recognizable as such. The glass correction is ground in a moderately smoked glass, the posterior surface of which is roughened light milk glass, leaving a clear area of from 4 to 5 mm. for the pupil. Exact pupillary distance is essential. A patient of mine who has a small remnant of peripheral detachment left in the only eye with vision, and who has refused to be operated on again, has worn such a glass for more than one and a half years. But the *Lochbrille* is very inconvenient on account of the restricted visual field. Therefore, the third method suggested would be by far the most practical one.

At present I am trying glasses which are only slightly roughened around the clear pupillary area, so that the patient sees through the other parts of the glass, but vision is somewhat foggy. They are less conspicuous than the other types of spectacles mentioned (fig. 5).

There is still another way to prevent detachment: an operation. I have not yet performed such an operation, but I believe that at some future time one will be able to detect the eyes in which the danger of detachment is imminent, and in these one would not hesitate to perform an operation.

It is self-evident, from all that has been said, that the spread of spontaneous detachment can be stopped in most cases by simple immobilization of the eyeball with the aid of the *Lochbrille.* This often prevents the formation of secondary, sometimes invisible, holes and thus assures a good prognosis for operation.

THE SUBRETINAL FLUID IN IDIOPATHIC DETACHMENT OF THE RETINA

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This article presents a study of the chemistry of the fluid which is met with in idiopathic detachment of the retina. It is customary to designate this fluid as a subretinal exudate, but this nomenclature is not scientifically exact, since the fluid lies between the layers of the pigmented epithelium and the retina proper. Both these layers of cells are sensory, and it would seem more exact to call the fluid an intraretinal exudate. The opinion that this subretinal fluid and the fluid which fills the vitreous have the same viscosity and the same percentage of albumin is attributed to Leber. The supporters of the so-called retention theory of idiopathic detachment, following the lead of Gonin, attribute the lifting of the retina (it would be more exact to say the folding of the retina) to a passage of vitreous through the tear which one sees in 80 per cent of these cases.

For a long time, however, the protagonists of the exudative theory have insisted on the albuminous character of the subretinal fluid. Rahlmann,[1] in 1893, reported a case in which the fluid contained 9 per cent albumin and in which 16.5 per cent of the solid residue was albuminous. He commented that it was unfortunate that certain other men who, like himself, had observed a high percentage of albumin in this fluid, had not mentioned the figure for the vitreous. In order to make a legitimate comparison this information is necessary. In 1912 Birch-Hirschfeld [2] reported a case of detachment of the retina of one year's duration in a myopic patient 42 years of age in which the exudate contained 2.6 per cent albumin. Though the literature discloses a few endeavors to elucidate the pathologic anatomy present in idiopathic detachment few studies of the serum have been reported. Jamamoto [3] reported retention of chlorides, and for this reason he concluded that the fluid was a choroidal transudate. Loewenstein [3a] estimated that the

1. Rahlmann: Arch. f. Augenh. **27:1**, 1893.
2. Birch-Hirschfeld: Arch. f. Ophth. **82:**26, 1912.
3. Jamamoto: Acta Japonica **34:**569, 1930.
3a. Loewenstein: Arch. f. Augenh. **70:**37, 1911.

subretinal fluid contained considerable albumin. In 1911, he studied the fluid obtained in three cases of detachment and reported the viscosity to be as follows:

Case	Viscosity		
	Blood Serum	Plasma	Retinal Fluid
1	1.9	2.25	2.3
2	1.75	2.0	2.15
3	1.9	2.2	2.25

In 1929, Baurmann[4] endeavored to develop a theory based on disturbed colloidal, osmotic and hydrostatic relationships. In reporting this work he mentioned the albumin content of the subretinal fluid in four cases:

Case	Albumin, Per Cent	
1	3.5	
2	8.3	
3	11.2	
4	0.12	(Detachment of seven days' duration)

He drew attention to the fact that one case (no. 3) showed a high percentage of albumin, 11.2 per cent, which represents a higher concentration of albumin than that of the blood serum.

In 1932, Magitot and Lenoir,[5] using microchemical methods, studied the subretinal fluid from the point of view of color and albumin and dextrose content. The data obtained are given in a later paragraph of this article, as are also the results of a study of the chlorides and certain other pathologic findings. In his recent treatise on detachment of the retina Arruga[6] devoted a chapter to the retinal fluid. This distinguished scientist believes that the retinal exudate closely resembles the vitreous in transparency and viscosity. He estimated the percentage of albumin in thirty-eight cases, either using a technic which utilized boiling or making his estimations by refractometry; he stated, as did Vogt, that the amount of albumin varies with the duration of the detachment, in general the percentage of albumin being lowest in the cases in which the detachment is most recent. Unfortunately the methods used in these experiments are open to criticism. In addition to the variations which may occur owing to coagulation when boiling is resorted to, refractometry gives very inexact results when it is applied to fluid which contains considerable amounts of sodium chloride. It is well known that the index of refraction of fluids varies not only

4. Baurmann: Arch. f. Ophth. **122**:15, 1929.

5. Magitot, A., and Lenoir, A.: Bull. et mém. Soc franç. d'opht. **45**:225, 1932.

6. Arruga: Rep. Internat. Cong. Ophth., Madrid, 1933, p. 89.

according to temperature but according to the quantity of electrolytes present; and the subretinal fluid contains large quantities of sodium chloride.

One of the widely accepted theories explaining the etiology of detachment of the retina is based on the idea that the subretinal fluid and the vitreous are of almost similar physicochemical composition. If one wishes to solve the question of the cause of idiopathic detachment of the retina it is necessary to have some exact information concerning the chemistry of the retinal fluid. One must know: (*a*) the chemical composition of the vitreous of the normal human eye; (*b*) the chemical composition of the vitreous in detachment of the retina, and (*c*) the chemical composition of the subretinal fluid.

The chemical composition of the vitreous of certain animals is well known. For the purposes of this paper I shall quote only the figures for albumin, sugar and chlorides. The albumin content, as given by several authorities, is as follows: Redslob,[7] 0.025 per cent; Jess,[8] 0.018 per cent (calves); Franceschetti,[9] 0.04 per cent (horses); Duke-Elder,[10] 0.065 per cent.

For the human eye I have reported the albumin content of the vitreous as being nearly the same as that of the aqueous humor, e. g., 0.028 per cent when the amount in the aqueous is 0.02 per cent.

The figures representing the dextrose content of the vitreous have no interest unless they can be compared with the results of a simultaneous estimation of the blood sugar. Sugar is a diffusible substance which passes freely from the blood to the aqueous and vitreous. The intake of sugar varies this figure considerably, and for this reason only carnivorous animals can be used in such experimentation.

Duke-Elder[11] gave the following figures for the horse: 98.3 mg. per hundred cubic centimeters of the vitreous when the sugar content of the blood is 91 mg. However, the research work of Francis Adler[12] gave the most exact knowledge of the dextrose content of the vitreous. Using the cat as an experimental animal, Adler arrived at the following figures:

	Sugar Content (Average), Mg. per 100 Cc.
Vitreous	64
Aqueous	113
Blood	135

7. Redslob, E.: Bull. et mém. Soc. franç. d'opht. **45**:293, 1932.

8. Jess: Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch., Jena **43**:11, 1922.

9. Franceschetti, A.: Arch. f. Augenh. **99**:367, 1928.

10. Duke-Elder: The Nature of the Vitreous Body, London, George Pulman and Sons, Ltd., 1930.

11. Duke-Elder, W. S.: J. Physiol. **68**:155, 1929.

12. Adler, F. H.: Tr. Am. Ophth. Soc. **28**:307, 1930.

Among other observations he pointed out that the normal retina has a high glycolytic power. He found that the percentage of sugar in the vitreous varies in different regions. The posterior layers contain less sugar than the anterior layers; for example, the central portion of the vitreous has a sugar content of 0.744 per cent, and the peripheral portion has a content of 0.688 per cent.

Magitot and Lenoir,[13] working with human vitreous, proved that the sugar content of the vitreous follows closely the sugar content of the blood. However, these authors found the same difference in sugar content between the central portion of the vitreous and the posterior portion as was reported by Francis Adler. A normal eye of a man 70 years of age, which was enucleated because of an ethmoidal tumor, was immediately frozen, and the fluid was subjected to analysis, with the following results:

	Sugar Content, Mg. per 100 Cc.
Peripheral portion of vitreous (average)	68.8
Central portion of vitreous (average)	74.4
Blood	103.0

Several days later, when the patient was moribund and in coma the other eye was enucleated and treated in the same manner. The results of the second analysis were in every way comparable to the first.

It is well known that the percentage of sodium chloride in the aqueous humor is slightly higher than that of the blood. This seems to be true of the vitreous also, as is shown by the following figures obtained by various authors.

	Sodium Chloride of Vitreous, Per Cent	
Cattle:	0.775	(Lohmeyer)
	0.743	(Cahn)
	0.73	(Jess)
	0.678	(Cohen, Killian and Metzger)
Pigs:	0.705	(Cohen, Killian and Metzger)
Horses:	0.656	(Cohen, Killian and Metzger)

Duke-Elder considers that the electrical conductivity is the same for the aqueous as for the vitreous and that the same changes follow tapping in the vitreous as in the aqueous humor; after a certain delay there are an augmentation of the albumin content and a modification of sodium chloride content in the inverse direction. Unfortunately the chemical composition of the vitreous in idiopathic detachment of the retina is not known.

13. Magitot and Lenoir: Bull. Soc. de biol. **110**:1251, 1932.

Loewenstein,[14] in 1926, considered that the albumin content of the vitreous was around 0.02 per cent; in contrast to this figure, he estimated, on the basis of viscosity, a much higher albumin content for the retinal fluid.

Guggenheim and Franceschetti [15] found a normal index of refraction for the vitreous in a few cases of detachment. The ignorance of these matters arises from the difficulty in procuring the indispensable material for study. The fluid can be removed only in the course of an operation, and the amount withdrawn is always small and can be used only in small quantities. Besides this, as has been mentioned, the vitreous differs in consistency in various regions: Behind the crystalline lens it is relatively fluid while in the posterior chamber it has the consistency of a gel impossible to aspirate; it is only in cases of a high degree of myopia and in the presence of inflammatory processes that the posterior portion of the vitreous becomes liquid. In certain cases of detachment with a transparent vitreous and even in cases of myopia of high degree the posterior portion of the vitreous may remain a gel, and in other cases the liquefaction is only partial and exists only in a limited area, corresponding to the zone of detachment. Twice I succeeded in removing a little of the subretinal fluid and a certain quantity of vitreous from the same eye.

MATERIAL AND TECHNIC

The specimens were removed during operation on patients suffering from idiopathic detachment of the retina. The wall of the globe was denuded; at a chosen point the sclera was excavated down to the choroid by means of a diathermic bistoury or a galvanocautery. After this wound had been meticulously dried, a needle connected to the end of a bent tube made of special glass was introduced through the center of one of these excavated areas, and the chamber was superficially pierced. The subretinal fluid was then aspirated. After all the fluid that it was possible to aspirate had been withdrawn the needle was pulled out and another needle of a caliber of 1 mm. was pushed in to a depth of 1 cm. This maneuver was checked by an assistant who with the aid of an ophthalmoscope observed the needle to be sure that it reached the vitreous; the fluid was then withdrawn in the same manner.

Determination of Albumin.—The albumin content was determined either by the method which Mestrezat and I [16] had previously utilized (trichloracetic acid) or by the well known Heller method. The latter method gave the better results, the quantity of albumin being relatively much increased.

Determination of Sugar.—In these determinations I used the method of Hagedorn Cole, following the technic of Francis Adler. In order that the results

14. Loewenstein: Arch. f. Ophth. **117**:131, 1926.

15. Guggenheim, I., and Franceschetti, A.: Arch. f. Augenh. **98**:448, 1928.

16. Magitot and Mestrezat: Cong. de physiol., Paris, 1920; Ann. d'ocul. **159**: 401, 1922.

could be compared with those of the determinations of the blood sugar the same method was used for the latter estimations, which were controlled by the method of Bertrand.

Determination of Chlorides.—The method of Charpentier-Volhard, adapted to microdeterminations, was used for the estimation of chlorides; the same method was employed for the determination of blood chlorides. To obtain more precise results, solutions of very feeble concentrations were used (hundredth-normal). At each determination the titers were verified. The buret was graduated to 0.01 cc. The method is as follows: In an Erlenmeyer flask are placed distilled water, 10 cc., and fluid to be examined, 0.1 cc., to which are added solution of silver nitrate (nitrogen = 4 cc.), pure nitric acid, 1 cc., and saturated solution of potassium permanganate, 1 cc. The last three preparations are added in order to destroy any organic material which may be present. The mixture is then shaken and heated in a water bath to 100 C. for ten minutes.

The fluid becomes decolorized; if there is no decoloration one adds a little pure dextrose. The flask is allowed to cool, and the precipitate of silver chloride is then filtered off. The filter should be rinsed twice. A few drops of a 10 per cent solution of ferric aluminum sulphate are added to the filtrate. The titration is then made, a solution of ammoniated sulphocyanate being used.

The reaction is indicated by a persistent rose color. If equal amounts of fluid have been employed, the figure obtained is subtracted from the figure found on titration and the difference is multiplied by 0.585; the number thus obtained indicates the percentage of sodium chloride in the fluid examined.

RESULTS

Coloration of the Retinal Fluid.—As is shown in tables 1 and 2, twenty-four specimens of retinal fluid were examined. In twenty-four instances the fluid was transparent, but in only five was it colorless; in nineteen instances it was xanthic. The five patients from whom the colorless liquid was obtained were suffering from detachments of varying duration: fifteen days, a month, six weeks, two months and a year and a half. The time for which the detachment has existed does not seem to be of any great importance in determining the color of the fluid, since in the nineteen cases in which the liquid had a yellow tinge the retinal detachment had existed for fifteen days, twenty days, two months, four months and longer. The xanthic tinge was not ordinarily found in the humors except when it might have been produced by a slight escape of blood. If a little fresh blood had been aspirated from the wound the color would have been reddish and not yellow and the pipet would have contained a stain.

Cholesterol.—Cholesterol was found only once in the twenty-four examinations and then in the form of crystals in a case of four months' standing. This substance, which indicates profound cellular changes, may nevertheless be found in relatively recent cases.

TABLE 1.—*Sugar Content of Subretinal Fluid and Blood*

Cases of Detachment	Sugar, Mg. per 100 Cc.		Albumin of Fluid, Mg. per 100 Cc.	Coloration of Fluid
	Blood	Retinal Fluid		
1. Woman, aged 24; detachment 15 days; refraction, —10; tear, ++	107	75	135	Yellow +
2. Man, aged 38; detachment 23 days; refraction, —8; tear, +	87	73	1,500	Yellow +
3. Man, aged 64; detachment 2 months; refraction, —8; tear, ++	100	78	1,000	Yellow +
Second operation 3 months later	158	140	1,500	Yellow +++
4. Man, aged 64; detachment 2 months; refraction, —4; tear, +	95	63	.....	Yellow +
5. Woman, aged 38; detachment 2 months; refraction, —6; tear, 0; no fluid could be drawn but with the needle pushed deeper some vitreous was removed	85	55 (vitreous)		
Second operation 2 months later	119	78	15,000	Yellow +++
6. Woman, aged 55; detachment 2 months; emmetropia; tear, +++	76	71	2,100	Yellow ++
7. Man, aged 18; detachment 2 months; refraction, —20; tear, 0	123	90	.....	Clear
8. Woman, aged 57; detachment 4 months; refraction, —3; tear, +	180	180	1,200	Yellow ++
9. Man, aged 70; detachment 4 months; refraction, —10; tear, +	107	90	6,000	Yellow ++
10. Woman, aged 52; detachment 4 months; refraction, —10; tear, +	122	120	3,000	Yellow +++

TABLE 2.—*Chloride Content of Subretinal Fluid and Blood*

Cases of Detachment	Chloride, Mg. per 100 Cc.		Albumin of Fluid, Mg. per 100 Cc.	Coloration of Fluid
	Blood	Retinal Fluid		
1. Man, aged 61; detachment 15 days; refraction, —10; tear, +	697	631	450	Clear
2. Woman, aged 43; detachment 20 days; refraction, —12; tear, +	755	663	750	Yellow ++
3. Woman, aged 53; detachment 30 days; emmetropia; tear, +	707	739	300	Clear
4. Man, aged 34; detachment 6 weeks; emmetropia; tear, +	748	592	450	Clear
5. Woman, aged 63; detachment 2 months; refraction, —12; tear, +	643	741	...	Yellow +
Second operation 4 weeks later	733	739	...	Yellow +
6. Man, aged 59; detachment 4 months; emmetropia; tear, +	771	704	3,000	Yellow +
Second operation 7 weeks later	707	745	2,250	Yellow +
7. Man, aged 38; detachment 6 months; emmetropia; tear, +	699	757	4,500	Yellow +++
Second operation 5 weeks later	738	723	2,200	Yellow +++
8. Man, aged 17; detachment 6 months; refraction, —11; tear, 0	699	697	1,500	Yellow ++
9. Woman, aged 19; detachment 1½ years; refraction, —8; tear, +	726	638	750	Clear
10. Man, aged 70; detachment 2 years; emmetropia; tear +	682	828	3,100	Yellow +++

Albumin.—In nineteen specimens of retinal fluid examined the albumin content was always high. The lowest amount found was 135 mg. per hundred cubic centimeters in a case of fifteen days' duration, but in another case of the same duration the content was 450 mg. In general, it seems that the quantity of albumin is proportional to the duration of the detachment, but this rule is far from being absolute; to convince oneself of this fact it is necessary only to note cases 2 in tables 1 and 2. In both these cases the detachment was of about twenty days' duration. On the other hand, the amount of albumin seems proportional to the intensity of the xanthic tint. In certain cases the quantity is exceptionally high (case 5, table 1), exceeding the albumin content of the blood serum. One must, then, conclude that these excessive quantities of albumin arise from a protoplasmic disintegration, not only in the blood corpuscles but in the nerve cells of the retina. This disintegration may be observed in studying the anatomic changes in detachment of the retina.

However this may be, the increase in albumin (and there is a relative increase even in the cases in which the content is lowest) is in direct contrast to the amounts of albumin which are found in the human vitreous. It is exceptional for the vitreous of a normal human eye to contain more than 100 mg. of albumin per hundred cubic centimeters. This is true also in inflammatory conditions, except in panophthalmia and hemorrhages. It holds true, moreover, for the human eye in spite of contrary observations which have been made for the rabbit and the cat. In any case the elevated percentage of albumin in the retinal fluid explains the toxic action of this fluid when it is reinjected into the vitreous (Deutchmann) of the same globe from which it was extracted. Under those circumstances it produces a protein shock reaction.

Dextrose.—The quantities of sugar found in the ten cases listed in table 1 should be compared with two standards, that of the normal vitreous and that of the blood. In a normal man having a blood sugar of 103 mg. per hundred cubic centimeters I found a dextrose content of 68 mg. in the peripheral portion of the vitreous and of 74 mg. in the central portion. These results are in absolute conformity with those which Francis Adler reported for the cat.

My studies of the retinal fluid showed that the dextrose content varied considerably. In case 10 in table 1 the amount of sugar in the fluid and in the blood was nearly identical. This patient had a recurrent detachment and had been operated on a year previously. The retina showed marked pathologic changes. In case 9 in table 1 the detachment was of recent date (only four months), but the patient was an old man in whom the retina showed pathologic changes as marked as those in case 10. The quantity of dextrose was 900 mg. per hundred cubic centi-

meters, while the blood sugar content was 107 mg. In case 8 the amounts of sugar in the blood and the retinal fluid were identical. On the other hand, in cases 7 and 1 the difference between the sugar content of the retinal fluid and that of the blood was considerable. In reviewing the results obtained in the ten cases under scrutiny it does not seem that the duration of the detachment has a direct bearing on the quantity of the sugar in the fluid; however, there appears to be a relationship between the ability of the retina to function and the quantity of sugar in the fluid.

This suggests that a retina which is profoundly disorganized has lost its glycolytic power, while nerve tissue which carries on its normal function continues to metabolize sugar in the course of the cellular activity which produces lactic acid. From this point of view the relation between the sugar content of the retinal fluid and that of the blood should serve as an indication of the physiologic condition of the detached retina. The comparative figures for the sugar content of the blood, the subretinal fluid and the vitreous which are given here were obtained in two cases in which it was possible to extract the retinal fluid and the vitreous at the same time. In the first case the detachment was of four years' duration; the patient had myopia of 10 diopters. The results were as follows: blood sugar, 122 mg. per hundred cubic centimeters; sugar, content of the retinal fluid, 120 mg., and sugar content of the vitreous, 82 mg.

One sees at a glance that there is a great discrepancy between the amount of sugar in the vitreous and that in the retinal fluid. It would be difficult to assume that these two fluids are of the same chemical nature.

Chlorides.—I have not been able to find anywhere in the literature a figure representing the chloride content of the human vitreous compared with that of the blood. In studies made by Lohmeyer, Cahn, Jess, and Cohen, Killian and Metzger[17] on animals the following figures were given: cattle and pigs, 700 mg., and horses, 696 mg., per hundred cubic centimeters.

Duke-Elder stated that the percentage of chloride of the vitreous is very near that of the aqueous. He added that under conditions which irritate the eye changes occur in the vitreous which parallel the modifications in the aqueous; i. e., when the albumin increases the chlorides diminish, and vice versa. With these facts in mind it was interesting to make comparative observations using my information concerning (1) the quantity of albumin, (2) the quantity of chlorides and (3) the comparison of the subretinal chlorides with the blood chlorides. This study is resumed in table 2. A study of this table discloses that in five cases the chloride content was found to be higher than that of the blood,

17. Cohen, Killian and Metzger: Proc. Soc. Exper. Biol. & Med. **22**:445, 1925.

and in seven cases, lower; the accepted rule for the vitreous and aqueous on which the equilibrium theory of Donnan depends was then in default seven times. If one compares the chloride content with the albumin content it is easy to remark that the inverse relationship between the amount of chlorides and the amount of albumin does not exist in the retinal fluid. There may be at the same time a large amount of chlorides and a relatively large amount of albumin, as in cases 6 and 7. If one attempts to find a relationship between the chloride content of the retinal fluid and the duration of the detachment, one is confronted by the fact that in recent cases the chloride content is sometimes greater and sometimes less than that of the blood. Neither does there seem to exist any parallelism between a high chloride content and the color of the fluid.

Aqueous Humor.—The six cases in which the aqueous humor was examined are listed in table 3. Unfortunately it was not possible to

TABLE 3.—*The Aqueous in Detachment of the Retina*

Cases of Detachment	Albumin, Mg. per 100 Cc.	Sodium Chloride, Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.
1. Woman, aged 19; detachment 1 month; refraction, —7; opacities of vitreous	12	730	85
2. Woman, aged 25; detachment 1 year; refraction, —12; opacities of vitreous	200	667	87
3. Woman, aged 45; detachment in retinitis albuminurica; hemorrhage; azotemia, 2.23	36	705	
4. Woman, aged 57, detachment 7 months; emmetropia; opacities of vitreous	225	660	
5. Man, aged 48; traumatic detachment 4 years; cataract; yellow aqueous	240	612	
6. Man, aged 27; sarcoma of choroid; no hypertension	50	715	

complete this study by a simultaneous study of the vitreous. In spite of this gap, these figures have an interest, since they may be compared with the results of studies in other cases in which the retinal fluid was analyzed. For example, in a case of retinal detachment of one month's duration in which there were mobile opacities of the vitreous, a study of the aqueous revealed normal amounts of albumin, sugar and chlorides.

I found that in long-standing cases the amount of albumin never exceeds 250 mg. per hundred cubic centimeters. This is a high figure which is never exceeded in the human aqueous even in cases in which the anterior chamber is repeatedly punctured. However, this figure is relatively small when compared to the albumin content of the specimens of retinal fluid that I have examined.

COMMENT AND CONCLUSIONS

In general the retinal fluid contains relatively large amounts of albumin. It is possible that the quantity is less in recent cases than in

cases of long duration. There appears, however, to be no exact rule governing this relationship. Arruga encountered exceptions to such a definite relationship just as I have done. On the other hand, the amount of albumin seems to have some relationship to the color of the fluid. When the fluid has a yellow tinge it usually has a high albumin content. There are cases in which the albumin content of the retinal fluid is higher than that of the blood serum.

Figure 1 is a photograph of a section of an eye taken from a young man suffering from retinal detachment of eight days' duration. As it was believed that the detachment was secondary to a tumor, the eye was enucleated, and it was possible to fix it in Zenker's solution under favorable conditions. The section shows that there was an idiopathic detachment which had extended along the whole expanse of the retina, making a voluminous pocket which enclosed considerable retinal fluid. The albuminous nature of this fluid was attested to on gross observation by the difference in tint between the contents of the sac and the vitreous. The same observation was made by Kuemmel,[18] who published the report of an anatomic examination of an eye enucleated because a tumor was thought to be present when in fact the case was one of idiopathic detachment. Other descriptions which exist in the literature (Gonin,[19] Sourdille,[20] Redslob,[21] Bartels,[22] Arruga[6]) are of little value because the detachments were either old or complicated by glaucoma or inflammatory conditions. Other observations, moreover, were made on eyes which were poorly fixed (Sourdille, Redslob, Gonin) or, as in the case of Bartels, on eyes which had been subjected to other interventions before fixing.

Frequently it was observed that the retinal fluid had a xanthic or yellow tinge; this results from an old small hemorrhage or a leakage of blood and appears more frequently in long-standing detachments than in those of short duration. However, case 2 of table 2 and cases 1, 2 and 3 of table 1 show that colored fluid may be found in recent cases. Since clinically one frequently observes small hemorrhages in cases of detachment of the retina, this fact should not be surprising. To judge accurately of the color of the fluid it is well to take the precaution of placing the tube which contains it against a dead white background.

The quantities of dextrose found in the retinal fluid are very variable. Experience has shown that in cases in which the retina has undergone considerable disorganization the amount of sugar in the

18. Kuemmel: Arch. f. Augenh. **100**:314, 1929.

19. Gonin: Bull. et mém. Soc. franç. d'opht. **33**:1, 1920.

20. Sourdille: Bull. et mém. Soc. franç. d'opht. **45**:235, 1932.

21. Redslob, E.: Bull. Soc. d'opht. de Paris, March, 1931, p. 211.

22. Bartels: Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch., Leipzig, 1932, p. 477.

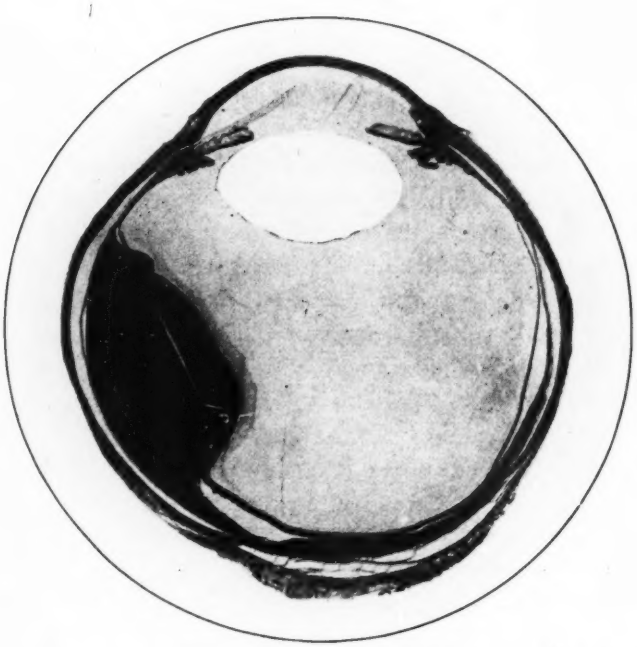

Fig. 1.—Section of a globe showing a recent detachment of the retina (eight days).

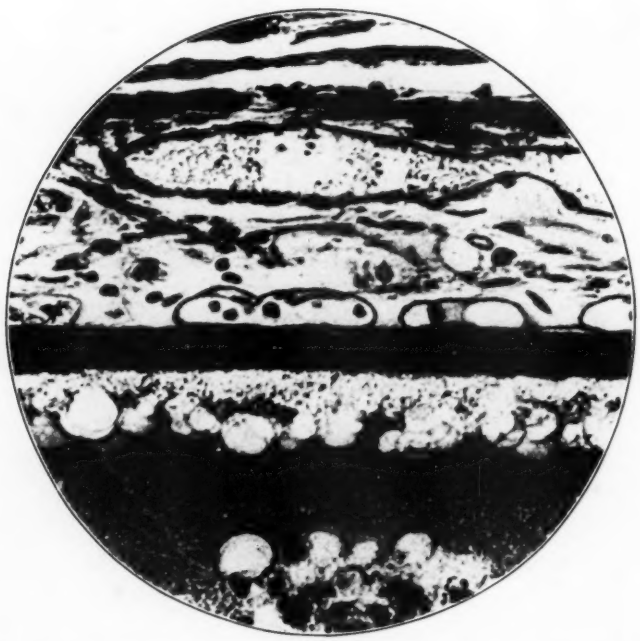

Fig. 2.—Same globe as in figure 1. Section showing the choriocapillaris, the pigment epithelium and the retinal fluid.

fluid is nearly the same as that in the blood. The dextrose content is less that that of the blood when the chambers are clear and the vision remains fair. These observations lead to the conclusion that there is a correlation between the physiologic state of the retina and the quantity of sugar found in the retinal fluid. When the retina has retained its glycolytic function, relatively little sugar is found in the retinal fluid, while when this physiologic function has disappeared larger amounts of sugar are present. From this point of view the percentage of sugar in the retinal fluid may serve as an indication of the functional state of the retina and permit one to make a prognosis of possible remaining function in cases in which surgical intervention is contemplated.

A study of the chlorides shows that the retinal fluid may contain more or less chlorides than the blood; five times in twelve determinations I found the content to be less than that of the blood. It is noteworthy that, contrary to the rule which governs the relative proportions of albumin and chlorides in the aqueous and vitreous, this inverse relationship between the amount of chlorides and the amount of albumin does not seem to exist in the retinal fluid. One may find at the same time a relatively large amount both of albumin and of chlorides. Finally, moreover, there exist cases, such as case 10 in table 2, in which the amount of chlorides in the retinal fluid is considerably higher than that in the blood and entirely out of proportion to the known composition of normal ocular fluids.

The retinal fluid in its chemical composition differs essentially from the vitreous in two respects: (1) The albumin content is considerably higher, and (2) the chloride content is often less than that of the blood serum, while the chloride content of the normal vitreous is usually slightly above that of the blood.

There does not exist in the retinal fluid the inverse relationship between chlorides and albumin which has been repeatedly observed in the vitreous and aqueous humors. The sugar content of the retinal fluid and of the vitreous of an eye in which retinal detachment existed were found to be different.

The chemical composition of the retinal fluid resembles that of an exudate. However, the fact that at times it may contain more albumin and more sugar than the blood serum should, it seems, lead to the conclusion that this fluid is not a simple exudate. The high content of solids points to the presence of products of cell disintegration. This hypothesis is confirmed by studies of the pathologic anatomy. The lesion is not greatest in the pigmented epithelium or in the capillaries of the choroid. The real seat of the lesion is in the layer of rods and cones. The destruction which begins here extends rapidly to the outer nuclear layer, i. e., to the layer of bipolar cells. Little islands of

degenerating cells increase very rapidly to form lacunae which, as they grow larger, assume the appearance of cysts. The protoplasmic débris of disintegrating cells falls into the fluid which accumulates between the visual cells and the pigmented epithelium. It is possible to distinguish detached nerve cells; some of them contain large vacuoles, while others are filled with pigment or remnants of nuclear phagocytes. This early degeneration of the visual cells explains why in so many cases of detachment in which the patient has been successfully operated on and to all appearances cured there persists a definite visual deficiency.

The serum, the chlorides and the albumin of this subretinal fluid appear to be derived as much from products of cellular disintegration as from the blood serum. The exudative origin is often attested to by the presence of minute hemorrhages on the retina. In following this line of thought it is important to take into account the fact that most authors who have reported the results of examinations of eyes in which detachment of the retina existed have remarked that the choroid was intact. Kuemmel reported that the choroid was normal in the case studied by him, and I, having had the occasion to examine sections from the cases studied by Redslob, Sourdille and Veil,[23] made the same observation. In addition, I had the opportunity to confirm this finding on an enucleated eye which was a particularly valuable specimen because the fixation was perfect. In this case also there was no lesion in the choroid; further, I was much struck by the excellent condition of the pigmented epithelium; the cells remained in a regular layer and the only signs of a pathologic condition were a slight swelling of the cells and, in places, the loss of pigmented fringes.

While one cannot perhaps entirely exclude the choroid as a source of the serous exudate which appears in the intraretinal spaces, it seems difficult in the face of many observations and of the comparative study of the subretinal fluid reported here, to concede that the whole of the exudate originates from the choroid. Further arguments against such a view are found in the pathologic picture. A study of sections convinces one that the lesions are greatest in the retina and that there are not even any suspicious shreds of fibrin in the vitreous. It seems to me preposterous, therefore, to envisage a vitreous rather than a retinal origin for this fluid.

This serous exudate is relatively low in albumin content when no hemorrhage has occurred, and the amount of protein and of chlorides increases in proportion to the amount of cellular disintegration present in the visual and the bipolar cells. As the pathologic process progresses certain cells disappear and their protoplasmic remnants become part of

23. Veil, P.; Dollfus, M. A., and Bousseau, M.: Bull. Soc. d'opht. de Paris, April, 1932, p. 235.

the accumulating fluid. The retina takes on the appearance of a cystic membrane. At certain places the walls of these cysts become so thin that a tear is produced. Such a picture explains the actual process in retinal detachment, but where shall one look for the primary cause of the injury to the nerve cells? There are many hypotheses which might be cited to explain the cause of this degeneration. If one recalls how frequently retinal detachment is bilateral and how often the thin areas seem to be situated in a region irrigated by branches of one larger vessel, and then takes into account the insignificant lesions of this character which are often met with in routine ophthalmic examinations, I think that one will search for the primary cause in a focus of infection or in the presence of some pathologic process resembling syringomyelia or syringobulbia. The operations which puncture the globe over the site of the tear seem to have a more favorable effect than others. The point of puncture is made at a place where the retina is thinnest, and the technic used permits the fluid to drain during several days.

PERSISTENCE OF CAPSULOPUPILLARY VESSELS

AS A FACTOR IN THE PRODUCTION OF ABNORMALITIES OF THE IRIS AND LENS

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The part played by undue persistence of portions of the fetal vascular system of the eye has long been recognized in considering the factors involved in the production of congenital anomalies. Indeed, one of the most striking phenomena in the whole developmental history of the mammalian eye is the elaborate formation of a complicated transient vascular system which disappears in adult life. These vessels are peculiar to mammals, only rudiments of them occurring in animals lower in the scale. They reach a very high stage of development in man, and their occasional persistence or abnormality is to be expected and is well known.

The transient vascular system referred to comprises the hyaloid artery and its branches (the outer and the inner set of the vasa hyaloidea propria and the terminal branches of the hyaloid on the back of the lens), the posterior vascular capsule of the lens, the lateral or capsulopupillary portion of this and the anterior portion or pupillary membrane. I wish to describe six cases illustrative of some of the various types of anomalies which may be produced by overdevelopment or undue persistence of the capsulopupillary (or iridohyaloid) vessels alone. In 1924, in a paper discussing the probable embryology of coloboma iridis, I [1] described their normal development and gave details of two cases of undue persistence in embryos. The present series of cases was observed in postnatal life, and they represent some of the probable final conditions of the embryonic cases described previously.

PREVIOUS OBSERVATIONS

Many embryologists (Bach and Seefelder,[2] Versari [3] and others) have called attention to the fact that the capsulopupillary (iridohyaloid) vessels indent the margin of the optic cup as they curl over it to

1. Mann, Ida C.: Coloboma Iridis and Its Embryology, Tr. Ophth. Soc. U. Kingdom **44**:161, 1924.

2. Bach, Ludwig, and Seefelder, Richard: Atlas zur Entwicklungsgeschichte des menschlichen Auges, Leipzig, Wilhelm Engelmann, 1911-1912.

3. Versari, R.: Le fasi di sviluppo e di regresso della tunica vasculosa lentis e la morfogenesi dei vasi sanguiferi nei processi ciliare e nell' iride dell' occhio dell' uomo, Ricerche di morfol. **3**:2, 1923.

anastomose with the vessels of the choroid via the annular vessel. Figure 1 *A* (after Bach and Seefelder) shows a coronal section of the margin of the optic cup of a human embryo with five such indentations. Figure 1 *B* shows a model of the optic cup of a mouse embryo with four notches around the margin, one of them in the region of the fetal cleft. Such notches are entirely normal in early stages, before the margin of the cup has grown forward to form the ectodermal layers of the iris. Normally, as this occurs the vessels atrophy and break away, and the margin of the cup becomes smooth and even again. If one or more such vessels persist, one may expect to find one or more corresponding notches or colobomas of the margin of the pupil. The vessel which caused the coloboma may later disappear, or some traces of it or of the anterior vascular capsule may remain. Bock,[4] Rum-

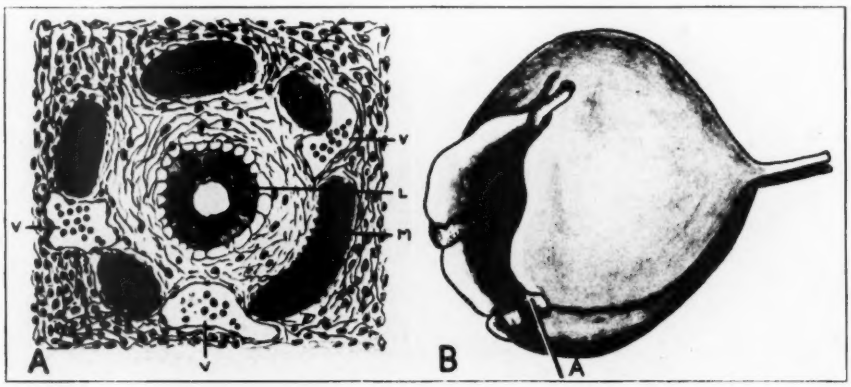

Fig. 1.—*A*, coronal section of the margin of the optic cup of a human embryo showing the indentations made by the capsulopupillary vessels. *V* indicates vessel; *L*, lens in section, and *M*, the margin of the cup. *B*, model of the optic cup of a mouse embryo with four notches around the margin, one of them (*A*) in the region of the fetal cleft.

schewitsch,[5] Plange,[6] Schön and others have noted the connection between coloboma iridis and persistent pupillary membrane. Plange, indeed, found the association in 42.9 per cent of cases of coloboma. Von Hippel[7] described in detail a case in which the lower part of the iris was thick and was pulled backward by a single large artery with muscular walls, which ran across the iris, bent around the pupillary margin between it and the lens and passed directly back into the

4. Bock, Emil: Die angeborenen Kolobome des Augäpfels, Vienna, J. Safář, 1893.

5. Rumschewitsch: Arch. f. Ophth. **37**:4, 1891.

6. Plange, O.: Arch. f. Augenh. **21**:194, 1890.

7. von Hippel: Arch. f. Ophth. **51**:130, 1900.

vitreous, where it broke up into branches. This seems to be a clear case of persistence of a capsulopupillary vessel.

It seems undoubted, therefore, that such an etiologic factor in the production of coloboma iridis exists, and it may prove interesting to examine the following clinical cases in detail for persisting evidence of the embryologic processes which produced the abnormality. In some the amount of abnormality is greater than in others, and this is probably correlated with the length of time that the vessel persisted.

REPORT OF CASES

CASE 1.—*Involvement of the Ectodermal Portion of the Iris.*—M. L., a woman, aged 39, stated that the sight in the left eye had always been defective; that in the right eye was good. On examination, there was some degree of amblyopia

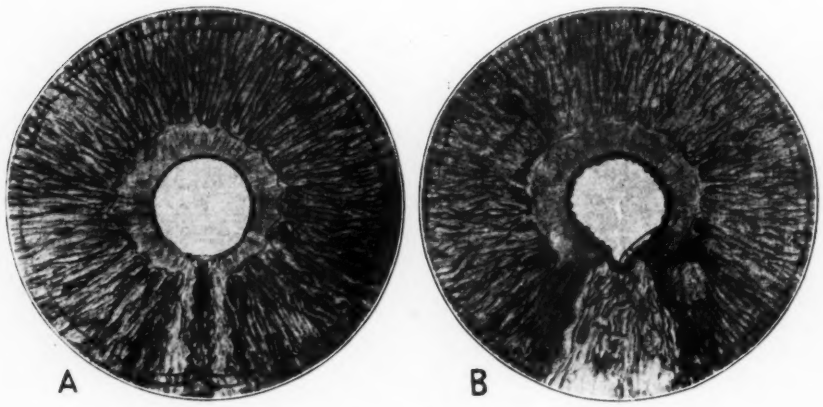

Fig. 2 (case 1).—Right and left eyes.

and myopia in the left eye, while the right was emmetropic. Both irides showed some abnormality. The appearance is indicated in figure 2. The iris and pupil of the left eye were normal, except at the lower part, where there was a small notch at the lower border of the pupil. This notch had a diameter, roughly, of only one sixteenth of the circumference of the contracted pupil. It was quite shallow, and there was no break in the uveal border of the pupil. On one side of the notch there was a fine strand of persistent pupillary membrane. The end of this was attached to the uvea at the apex of the notch. Below the notch the iris stroma was practically normal, except that in places its texture was more fluffy than elsewhere and the lesser circle was not distinguishable. In this area there were also six very small stroma vessels in which the color of the blood column could be seen. The maximum abnormality in this region was in the uvea. The posterior pigmented layers of the iris appeared to be entirely absent over the sector corresponding to the notch, the iris being translucent to retro-illumination with the slit lamp. Only a narrow band of uveal pigment was present just at the margin of the pupil.

The right eye of the same patient showed a similar condition in that the uveal layers were poorly developed below. There was a gap below in the uveal border

of the pupil, and the lesser circle ran inward to the margin of the pupil. The blood column was visible in two vessels of the stroma. There was no actual notch in the edge of the pupil or persistent pupillary membrane. The changes in this eye were so slight that they might have escaped notice but for the condition of the left eye, which served to explain them.

CASE 2.—*Involvement of the Mesodermal Iris and the Shape of the Pupil.*—E. G., a boy, aged 7, was said to have had an abnormal appearance of the right eye since birth. The delivery was instrumental, and the head was bruised, but the eye was not injured. The present condition was noticed immediately. The left eye was normal except for simple hypermetropic astigmatism with the rule.

When the right eye (fig. 3) was inspected, it was at once noticed that the pupil was slitlike and resembled that of a cat. The long axis of the slit was not, however, quite vertical, but was inclined downward and inward at an angle of about 30 degrees with the vertical. The uveal border was normal, except at the ends of the slit, where it was replaced by a whitish fibrous tissue. The iris stroma

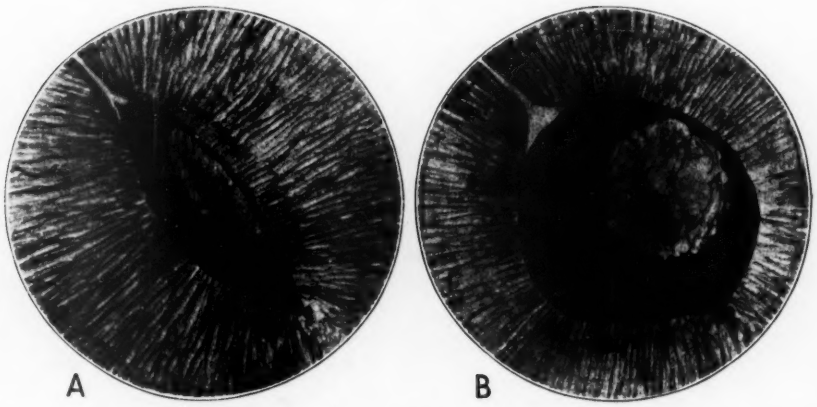

Fig. 3 (case 2).—The right eye. *A* shows the undilated pupil; *B*, after the instillation of atropine.

was thin and grayish, and the lesser circle could not be recognized; it probably coincided with the margin of the pupil. The pupil reacted to light by narrowing and widening of its shorter diameter. On the instillation of atropine, further abnormalities became apparent. The pupil became nearly circular, and the white fibrous tissue at the apexes of the slit was seen to be adherent to the lens so that these points remained fixed and the rest of the pupil dilated to them.

There was a central opacity in the lens involving all layers, and the lens was thinner and more flattened than normally. In three positions on the back of the lens, near the equator, were patches of uveal pigment which represented points of adhesion of ciliary processes to the lens. Through the upper apex of the slitlike pupil a thick strand of dense white tissue ran through the iris, replacing the stroma, to the limbus.

Comment.—If one attempted to offer an embryologic explanation, one would say that the abnormality began between the fourth and fifth months with undue persistence and toughness of two capsulopupillary

vessels corresponding to the apexes of the final slitlike pupil. These vessels became adherent to the lens and hindered the growth forward of the iris in these two situations, so that the width of the iris is only that of a 5 month eye, the rest of the iris being of normal width. The abnormality is thus to be looked on as two incomplete colobomas of the iris opposite each other, rather than as an atavistic attempt at

Fig. 4 (case 3).—Result of a single persistent capsulopupillary vessel.

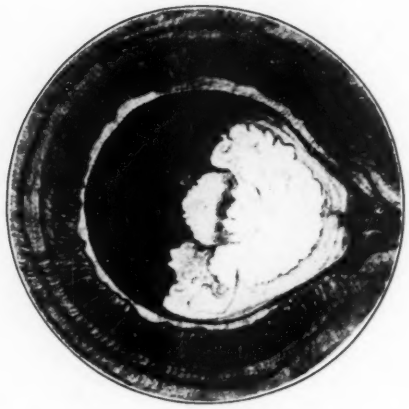

Fig. 5 (case 4).—Coloboma of the iris.

development of a vertical pupil. The adhesion of the ciliary processes to the lens is also an expression of retardation and anomaly at about the fourth month. The white strand across the iris in the upper part is probably a thickened vessel of the pupillary membrane in connection with the abnormal capsulopupillary vessel. That other portions of the hyaloid system may also have persisted is indicated by the fact that in spite of the opacity of the lens, a large number of whitish spots and strands can be seen in the vitreous. This case, therefore,

represents a further stage of the same sort of anomaly as that seen in case 1, in that the notching of the margin of the pupil is much deeper (and also, incidentally, occurs in two places) and there are adhesions to the capsule of the lens and interference with the growth of the lens. In the following cases, the condition has passed a stage further, in that the growth of the iris in the sector involved has been inhibited altogether, and the abnormality of the lens is more marked. These four cases are cases of involvement of the lens and of the mesodermal and ectodermal portion of the iris.

CASE 3.—In figure 4, the complete picture of the result of a single persistent capsulopupillary vessel is shown. There was a complete coloboma of the iris below, together with a coloboma of the lens and a gap in the fibers of the suspensory ligament.

Fig. 6 (case 5).—Large inferior coloboma of the iris and choroid and a small coloboma of the lens.

The nasal edge of the coloboma showed a fine strand of pupillary membrane attached to the lesser circle. The temporal edge showed slight overlapping of the ectodermal by the mesodermal portion.

The coloboma of the lens was of great interest. If one examines the gap in the suspensory ligament which lies opposite the notch in the equator of the lens, one sees a dense, sharply defined, pigmented strand of tissue, about the size of a large vessel. This strand runs from the limbus backward and curves around the equator of the lens, lying in the notch and being actually adherent to the lens. It is obvious that this strand was responsible for the notching of the lens and the failure of the zonule. It is undoubtedly a capsulopupillary vessel, and it bears a remarkable resemblance to that described by von Hippel.[7]

CASE 4 (fig. 5).—N. F., a woman, aged 21, was highly myopic. The coloboma of the iris was in the horizontal meridian, and there was a corresponding gap in the lens. In the gap could be seen a densely pigmented strand of tissue passing backward from the limbus. No suspensory ligament fibers could be seen. The edge of a ciliary process was visible in the lower part of the notch. There was a large laminated opacity of the lens involving about half the lens on the same

side as the notch. Undoubtedly, the anomaly was that of inhibition of the growth of the iris by a persistent capsulopupillary vessel, which also interfered with the nutrition of the lens.

Case 5 (fig. 6).—E. A., a woman, aged 41, had a large inferior coloboma of the iris and choroid (not involving the disk) and a small coloboma of the lens in the same situation. The suspensory ligament could not be seen in the gap. The interest in the case lay in the abnormality of the capsule of the lens, which bore definite evidence of a persistent pupillary membrane. The visible portion of the anterior capsule was peppered with stellate pigment cells. These cells were irregular in the central portion, but in the lower part, in the gap in the iris, they showed a regular linear arrangement. They formed six lines, running from the margin of the lens and converging toward the center of the pupil, which they did not quite reach. These lines of cells undoubtedly marked out the contact of the vessels with the lens at an earlier period. The vessels had disappeared, but the fact that their former position was marked by mesodermal cells showed that they

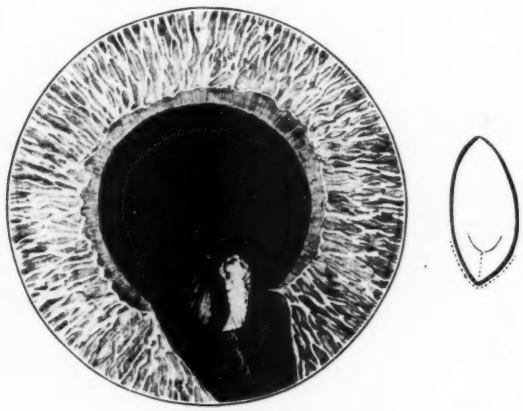

Fig. 7 (case 6).—Coloboma of the choroid, lens, iris and suspensory ligament. The small drawing at the side shows the position of opacities of the lens in section.

probably persisted too long and were responsible by their pressure for the gap in the iris and the notching of the lens.

Case 6.—The condition of the eye of E. C., a woman, aged 24, is seen in figure 7. This case is of extreme interest from an embryologic point of view, as it illustrates so well the way in which past events in embryonic life can be detected and placed in time by the traces which they leave. The case is one of coloboma of the choroid, iris, lens and suspensory ligament due to undue persistence of a single vascular strand in the position of one of the inferior capsulopupillary vessels. It will be best to describe each of the structures involved in order.

The iris showed a complete coloboma downward. At one point only, at the edge of the coloboma, a small tag of persistent pupillary membrane was adherent to the anterior capsule of the lens and to the lesser circle. The latter ended at the margins of the coloboma. Elsewhere the stroma of the iris was of normal appearance. The uveal border was normal and was continuous along the edges of the coloboma.

There was a small gap in the suspensory ligament of the lens corresponding to the center of the coloboma of the iris, but the edge of the lens was not notched.

The lens showed the most interesting changes. The main mass of the lens was clear. The size, shape and outline were normal (i. e., there was no coloboma or flattening). On the posterior capsule of the lens there were faint opacities, slightly to the nasal side of the posterior pole, and therefore corresponding in position with the termination of the hyaloid artery and probably connected with it. There was also a line of light brown pigmented dots, starting on the anterior capsule of the lens below the center and running downward to the equator, curving around this and running up on the posterior capsule for about the same distance. This line of dots resembled the lines of stellate cells seen in case 5, but only one line was present and was continuous over the equator onto the posterior surface.' It was situated opposite the center of the coloboma and undoubtedly corresponded with the line of one of the capsulopupillary vessels and its anterior continuation into the pupillary membrane. It passed around the equator of the lens through the gap in the suspensory ligament, and the inference was obvious that the vessel which caused the line also interfered with the development of the zonule. On examining the deeper layers of the lens, a curious dense, white, shell-like opacity was found on the surface of the fetal nucleus which was well marked off from the more superficial layers of the lens. This opacity was in the form of a band, wider than the line of brown dots, but corresponding with it exactly in position, only lying on a deeper plane within the lens. It wrapped around the equator of the fetal nucleus (much as would a very broad "rider" around the central opacity in a case of lamellar cataract) and ended bluntly, in front and behind, in a slightly broadened and irregular mass. This opacity seemed to be the original impress of the persisting vessel on the growing fibers of the lens. The vessel lay against the fetal nucleus in this situation during the fourth month and as it atrophied left its mark also on the capsule of the lens, which (by growth of the lens) became separated from the deeper opacity during the latter part of fetal life and during postnatal growth. Finally, a faint row of blue dots (similar to those of cataracta punctata cerulea) connected the equatorial portion of the deep white opacity with the equator of the lens opposite the gap in the zonule. This probably marked the point of maximum pressure.

Comment.—This case shows the stages of retrogression of the vessel. At the fourth month it was strong and dense, and its pressure was sufficient to cause damage to the underlying lens fibers and to prevent the development of the zonule. From then onward it stretched and atrophied, but some mesodermal cells from its walls remained on the capsule and became pigmented, probably at or soon after birth. The vessel is not to be seen, but one can compare its effects with the *Kalk,* "collarstud" or reduplication cataract that is known to occur after a localized disturbance of the growth of the lens or a slight injury in early life, the deep opacity representing the originally injured fibers of the lens which were later separated from the superficial imprint on the capsule by the subsequent growth of normal fibers. Since the pathologic process of reduplication cataract is so well known, the argument in favor of the presence of an abnormal vessel at the fourth or fifth month is almost irresistible.

COMMENT

The six cases reported bring out the following points with regard to the anomalies produced by the undue persistence of capsulopupillary vessels:

1. The persisting vessel can occur in any situation.

2. There is always a gap or a notch in either the ectodermal or the mesodermal portion of the iris, or in both.

3. Evidences of a persisting pupillary membrane will be found, either as tags from the lesser circle or as pigmented spots on the anterior capsule of the lens.

4. If the zonule can be seen, there will be a gap in it.

5. There is usually, but not always, a notch in the margin of the lens.

6. There is often, but not always, an opacity in the lens localized to the region of the coloboma.

7. The persisting vessel can sometimes be actually seen, but more often it has atrophied after having produced the various abnormalities.

COMPARATIVE RESULTS IN THE EXTRACTION OF SENILE CATARACTS

USING THE COMBINED, SIMPLE AND KNAPP-TÖRÖK INTRACAPSULAR METHODS

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This report of 450 cases of extraction of senile cataract is offered as a study of the comparative results obtained by the use of the combined, simple and intracapsular methods of operation and is in no way a brief for any one procedure. Each method of operation was used in 150 cases. The cases in which the combined method was used were all from private records; those in which the simple method was used were from private and clinical records, and those in which the intracapsular method was used were all from clinical records. The clinical records were from the ophthalmological department of the University of Michigan.

The cases selected for the simple operation were presumably uncomplicated; the corneas were large, the pupils were dilatable and the patients were well behaved. The cases selected for the intracapsular operation (performed according to the Knapp-Török method) were presumably uncomplicated; the patients were at least 60 years of age and were under good control; the eyes were not prominent, the corneas were large, and the pupils were dilatable. When the capsule ruptured the case was not included in the combined series, and cases with accidental extractions in the capsule were excluded from the series in which the intracapsular method was used. In each instance the classification, made prior to operation, was adhered to. A large incision, including a conjunctival flap, was attempted in every case, and no sutures, either corneal or conjunctival, were employed. The anterior chamber was irrigated in the cases in which operation by the simple or the combined method was used, unless there was a loss or impending loss of vitreous.

In table 1 the actual visual result in each case is given, together with the number of cases of loss of vitreous, prolapse of the iris and infections.

It is possible that refraction was determined later in the private cases than in those from the clinic, and that for this reason the average results are better in the combined group than in either of the other series.

All cases of loss of vitreous, however slight, are included in this report. In the group in which the combined method of operation was used it occurred three times, or in 2 per cent of the cases; in the cases in which the simple method was used, it occurred five times, or in 3.3 per cent, and in the cases in which the intracapsular method was used it occurred nine times, or in 6 per cent. In no case was loss of vitreous a demonstrable factor in the visual results obtained.

In the cases in which the combined method of operation was used prolapse of the iris occurred twice, or in 1.3 per cent; in the cases in which the simple method was used it occurred six times, or in 4 per cent,

TABLE 1.—*Visual Results in Each Case, with the Number of Cases of Loss of Vitreous, Prolapse of the Iris and Infections*

	Vision								
	6/4	6/5	6/6	6/7.5	6/12	6/15	6/30	6/60	6/60–
Type of Operation	Number of Cases								
Combined	5	14	35	60	11	12	5	2	6
Simple	0	19	48	35	14	8	15	3	8
Intracapsular	5	23	20	53	12	13	2	8	14

	Number of Cases		
	Loss of Vitreous	Prolapse of the Iris	Infections
Combined	3 (2%)	2 (1.3%)	1
Simple	5 (3.3%)	6 (4%)	1
Intracapsular	9 (6%)	3 (2%)	1

TABLE 2.—*Comparison of Visual Results*

	Per Cent of Total Number of Cases		Per Cent of Cases After All Pathologic Conditions Were Eliminated	
Type of Operation	Vision of 6/12	Vision of 6/15	Vision of 6/12	Vision of 6/15
Combined	83.3	91.3	87.4	95.8
Simple	77.3	82.6	87.2	93.2
Intracapsular	75.3	84.0	84.3	94.0

and in the cases in which the intracapsular method was used it occurred three times, or in 2 per cent.

There were three cases of infection, one in each of the series, or 0.7 per cent of the total of 450 cases.

A comparison of the visual results obtained was based on the number of cases in each series in which vision was 6/12 or better and those in which it was 6/15 or better, the calculations being based on the entire number of cases in which the operation was performed. Comparison was also made of the cases in which vision was 6/12 or better and those in which it was 6/15 or better in the cases remaining after all demonstrable pathologic conditions that might contribute to faulty vision were eliminated. The results obtained are shown in table 2.

It may be noted that the relative results of visual acuity of 6/12 or better were: with the combined method of operation, 83 per cent; with the simple method, 77 per cent, and with the intracapsular method, 75 per cent. For visual acuity of 6/15 or better they were: with the combined method, 91 per cent; with the simple method, 82 per cent, and with the intracapsular method, 84 per cent. After the elimination of all pathologic conditions that might account for the fact that vision was below the accepted standard, the results of vision of 6/12 or better were: with the combined method of operation, 87 per cent; with the simple method, 87 per cent, and with the intracapsular method, 84 per cent; while for vision of 6/15 or better they were: with the combined method,

TABLE 3.—*Pathologic Conditions Eliminated*

	Type of Operation		
	Combined	Simple	Intracapsular
Corneal scars	..	2	..
Vitreous degeneration	2	3	1
Optic atrophy	..	3	2
Venous thrombosis	1	..	..
Retinitis pigmentosa	..	1	1
High myopia	1	1	..
Detachment of the retina	..	1	2
Choroiditis	4	1	7
Refraction not completed	..	5	3
Total	8	17	16

TABLE 4.—*Relation of the Number of Secondary Cataracts to the Number of Operations Performed*

Type of Operation	Total Number of Secondary Cataracts	Number of Operations
Combined	34 (22.7%)	27
Simple	48 (32%)	15
Intracapsular	8 (5.3%)	6

95 per cent; with the simple method, 93 per cent, and with the intracapsular method, 94 per cent.

The demonstrable pathologic conditions that were eliminated in determining the visual acuity obtained in the uncomplicated cases are shown in table 3.

That the number of the demonstrable pathologic conditions deducted was less in the cases in which the combined method of operation was performed than in the other groups may be accounted for in part by the fact that all the cases in which operations by the combined method were performed were from private practice. Perhaps I was particularly fortunate in the cases in which the combined method of operation was used or unfortunate in the other groups. The only definite conclusion that can be drawn from the results already given is that cases which are uncomplicated cannot be selected in every instance.

SECONDARY CATARACTS

Table 4 shows the total number of secondary cataracts recorded, together with the number of operations performed.

In no case was the operation for secondary cataract followed by a serious reaction.

I shall not give the visual results following the secondary operations except in the group in which the intracapsular method was used. There was thickening of the hyaloid membrane in eight cases; in six cases operation gave the following visual results:

6/6	6/7.5	6/15	6/30
1	3	1	1

The patient with 6/30 vision had advanced choroidal changes. The record of the patient with 6/15 vision was incomplete so far as observations on the fundus were concerned.

There were two deaths, one from pneumonia and one from tuberculosis and pneumonia.

These results are offered not in the belief that they warrant definite conclusions, but rather as a contribution to the united experience of those who are studying the comparative results obtained by various methods of extraction.

Dr. C. W. Lepard, of Detroit, gave valuable assistance in the compilation of these records.

LAEVO-GLAUKOSAN AND EPINEPHRINE BITARTRATE IN THE TREATMENT OF GLAUCOMA

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Each year sees the advent of new ophthalmic drugs, only a few of which are worthy of a permanent place in the ophthalmologist's cabinet. Among these are certain concentrated solutions of epinephrine or synthetic preparations of a similar nature which seem to be proving of real value in selected cases of glaucoma.

It was my intention to review fully the history of the introduction and use of these drugs because such a review has not appeared in English, but it has recently been so excellently carried out in German by Thiel [1] and also by Peters [2] that my analysis would be scarcely more than a translation from these authors and as such seems hardly worth while. Suffice it to record here that soon after the isolation of the active principle of the suprarenals many ophthalmologists began to study its effect on the eye, and to mention briefly some of the more important studies along these lines. For a more complete consideration, reference should be made to the reports of Thiel and Peters, and the symposium at the Thirteenth International Congress at Amsterdam in 1929.

The physiologic action on the normal eye was pointed out by Wessely [3] and others. Probably the drug acts directly on the muscle cells of the dilator muscle of the pupil or on the sympathetic ganglion cells which lie within it. Darier [4] seems to have been the first to point out the tension-lowering effect on the glaucomatous eye, and he immediately recommended its use in combination with miotics.

Erdmann,[5] in 1914, was the first to use epinephrine subconjunctivally in glaucoma, having observed a tonometrically notable protracted

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Laevo-glaukosan has not been accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

1. Thiel, R.: Konservative Behandlung des primären Glaukoms: Adrenalin, in Schiek, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 4, p. 783.

2. Peters, A.: Das Glaukom, in Axenfeld and Elschnig: Handbuch der Augenheilkunde, ed. 3, Berlin, Julius Springer, 1930.

3. Wessely, K.: Ueber die Wirkung des Suprarenins auf das Auge, Verslg. d. ophth. Gesselsch., Heidelberg **28**:69, 1900.

4. Darier, cited by Löhlein, W.: Zentralbl. f. d. ges. Ophth. **22**:1, 1929.

5. Erdmann, P.: Ueber die Wirkung fortgesetzter subconjunctivaler Injectionen von Neben-nierenpräparaten beim Kaninchen und ihre therapeutische Verwendung beim Menschen, Ztschr. f. Augenh. **32**:216, 1914.

diminution of tension after its application. Since he saw an occasional elevation of tension following its use, he recommended it for chronic simple glaucoma only, and not for inflammatory conditions.

For some years little notice was taken of these publications, but after the World War, Knapp,[6] Hamburger,[7] Thiel,[8] Gradle,[9] and others began to make observations on the action of this drug. Hamburger was the most persistent in using it and in efforts to improve the preparation. In 1926, he brought out a formula that supposedly would eliminate the occasionally noted unfavorable reaction of solutions of epinephrine. He called this laevo-glaukosan, a combination of epinephrine (a twenty-fold combination of the usual solution) with an addition of 2 per cent methylamino-acetocatechol, dispensed in ampules because of the rapid deterioration to which epinephrine is subject. Hamburger recommended from three to five instillations at intervals in an hour. Owing to many reports of acute rises of tension following its administration, he accepted Gifford's[10] suggestion of using physostigmine (eserine) before and after the instillation of glaukosan. Hamburger[11] also brought out amin-glaukosan, which was a powerful miotic, but also a very painful one.

In 1924, Thiel suggested the use of epinephrine bitartrate in the form of a salve in concentrations from 1 : 100 to 1 : 1,000. In the last few years this drug has been prepared synthetically in powder form in ampules by Metz.

The primary action of laevo-glaukosan and epinephrine bitartrate, that of causing a fairly rapid fall in tension, in cases of chronic simple glaucoma is due to anemia induced in the vascular bed. The prolonged

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6. Knapp, A.: Action of Adrenalin in Glaucomatous Eye, Arch. Ophth. **50**: 556, 1921.

7. Hamburger, C.: Glaukosantropfen, Glaukom und Akkommodation, Klin. Monatsbl. f. Augenh. **76**:400, 1926.

8. Thiel, R.: Zur Wirkung des Adrenalins auf den Binnendruck des Glaukomauges, Klin. Monatsbl. f. Augenh. **72**:534, 1924; Klinische Untersuchungen zur Glaukomfrage, Arch. f. Ophth. **113**:319, 1924; Die medikamentöse Beeinflussung des Augendruckes, Verslg. d. ophth. Gesellsch., Heidelberg **44**:118, 1924; Experimentelle und klinische Untersuchungen über den Einfluss des Adrenalins auf den Augendruck beim Glaukom, Arch. f. Augenh. **96**:34, 1925; Zur medikamentösen Behandlung des Glaukoms, Berl. Fortbildungskurs für Augenärzte, Berlin, 1925, p. 66.

9. Gradle, H. S.: Epinephrin in Ocular Hypertension, J. A. M. A. **84**:675 (Feb. 28) 1925; The Use of Adrenalin in Increased Intraocular Tension, Am. J. Ophth. **7**:851, 1924.

10. Gifford, S. R.: Acute Rise of Tension Following the Use of Adrenalin in Glaucoma, Am. J. Ophth. **11**:628, 1928; Some Modern Preparations Used in the Treatment of Glaucoma, Arch. Ophth. **57**:612, 1928; Some Non-Surgical Aids in the Treatment of Glaucoma, Brit. J. Ophth. **13**:581, 1929.

11. Hamburger, C.: Das stärkste Miotikum, Klin. Monatsbl. f. Augenh. **76**: 849, 1926.

lowering of tension is probably due to a temporarily improved metabolism of the eye.

Since there seems to be no need for a complete review of the subject, I shall confine the paper to my personal experience with glaukosan and epinephrine bitartrate, giving an opinion as to the place of these drugs in ocular therapeusis and indicating how far this opinion coincides with that of others.

My first experience was with amin-glaukosan.

CASE 1.—In December, 1926, J. O., a white man, aged 47, came to the outpatient department of Washington University Medical School. There were moderate cupping of the right disk and marked cupping of the left disk. Vision was 20/50 in the right eye and 0 in the left; tension in the right eye was 64 mm. of mercury and in the left, 75 mm. (Tension readings noted in this paper were made with the Schiötz tonometer.) Iridectomy was performed on the right eye, which reduced the tension to 10. Four months later there was acute glaucoma in the right eye with a tension of 36, which yielded somewhat to miotics. On April 2, there was another acute attack in which the tension was 55. One drop of amin-glaukosan, 10 per cent, was instilled after cocaine anesthesia. It caused intense pain and desquamation of the entire superficial epithelium. The pain was excruciating, lasting four hours, but was followed by entire relief for three days, the tension of the eye being soft to the fingers. There was a little hardness on the fourth day. One week later the tension was 80. Amin-glaukosan was used again with temporary relief. The contraindication was the violent reaction and the nauseating pain, quite uncontrolled by morphine. The experience was so disturbing that I have never used this drug again.

Soon after this I began to use laevo-glaukosan rather frequently and later shifted to epinephrine bitartrate. In using the former, I employed four instillations at intervals of fifteen minutes after anesthetizing the eye with holocaine, 1 per cent, used three times at intervals of three minutes. I make only one instillation of epinephrine, after using holocaine as outlined. In some cases I have prescribed epinephrine bitartrate for use at home, always having the patient anesthetize the eye before use. I use either a 1 or 2 per cent solution of epinephrine, depending on the reaction. The powder will keep indefinitely in the unopened ampule, but the solution will slowly lose its potency so that after about three weeks it will be only about one half as efficacious as when first made. It should be kept in an icebox at a low temperature. It is possible to preserve the powder even after the ampule has been opened by tightly stoppering the ampule with cotton.

Glaukosan has been used in full strength just as it is prepared in liquid form in the ampule. One argument in favor of epinephrine is that it costs much less than glaukosan.

These drugs were tried in a few cases of acute uveitis in which there was no hypertension but in which the pupil failed to dilate with atropine and cocaine. In such cases the effect was sometimes good, but in gen-

eral no great benefit was thought to have been derived. An example of this is found in case 2.

CASE 2.—Mr. C. S. P., aged 46, had severe iridocyclitis in the left eye, of one month's duration. There was a gelatinous exudate in the anterior chamber, and vision was reduced to 2/240. Atropine and cocaine and 10 per cent ethylmorphine hydrochloride (U. S. P.) were used vigorously for one week; the pupil then measured 5 mm., and the tension was 21 mm. of mercury. Fifteen minutes after one instillation of 2 per cent epinephrine bitartrate, the pupil measured 7 mm., but after the lapse of an hour it again measured 5 mm. On the following day there was considerable pain; the pupil measured 6 mm., and the tension was 21. Two days after this, the pupil had contracted to 4.5 mm. It was felt that epinephrine had not proved advantageous. Three days later, under the original treatment with cocaine, atropine and ethylmorphine hydrochloride, the pupil was widely dilated.

I have had no personal experience with glaukosan and epinephrine in acute glaucoma, because the reports of others were so unanimous in condemnation that I never experimented with it. The occasional rise in tension following its use is an obvious contraindication in such cases.

Secondary glaucoma presents a somewhat different situation, in that occasionally these drugs will prove of benefit, though more often in my hands they have been ineffectual. A few illustrative cases of the action in various types of secondary glaucoma will be given, as they throw light on the kind of case in which there is some hope for success.

CASE 3.—Mr. H. B. P., aged 50, came to the office on April 1, because of a severe attack of iridocyclitis in the right eye. The Wassermann reaction of the blood was positive. There had been an attack of this kind, but less severe, in the left eye two years previously. Vision in the right eye was reduced to the perception of hand motions. Treatment was instituted with the applications of strong solutions of atropine, cocaine and ethylmorphine hydrochloride, and on April 15 the patient was in great pain, requiring morphine; the tension was 33. Atropine and cocaine were discontinued, and pilocarpine was used strenuously. On April 28 the tension was 32, and vision was limited to hand motions as before. An instillation of 1 per cent epinephrine bitartrate was made, after which the patient became faint. On the following day the pupil remained contracted, and the tension was 35.

CASE 4.—K. T., a Negress, aged 40, had iridocyclitis, keratitis and secondary glaucoma. On May 8, the tension was 40; on May 10, it was 48, and three days later, 43. On May 12, 2 drops of epinephrine bitartrate were instilled, and twenty minutes after the instillation the tension was 40; three days later it was 52. The medicament was used only once, but had no effect on this secondary glaucoma.

These two cases of glaucoma secondary to iridocyclitis showed no benefit from epinephrine and suggest that this type of case need not be expected to yield good results.

CASE 5.—A. G., a white woman, aged 62, had glaucoma secondary to needling of a postcataractous membrane. On January 3, the tension was 65; vision with glasses was 6/20. Epinephrine bitartrate was instilled five times. On January 10, the tension was 52. Epinephrine was used again, and the tension decreased on the

same day to 48. On January 17, the tension was 52. Epinephrine was used again in the same way. On January 24, the tension was 65. The use of strong physostigmine for three months did not lower the tension.

This case calls to mind the statement of Vannas [12] who, reporting in 1926 the action of glaukosan in sixty-one cases of glaucoma, said that the drug was not effectual in cases in which the tension had been over 40 and in general was not satisfactory in anything but chronic simple glaucoma.

The next case illustrates a partial success in a case of very high tension with much pain associated with severe intra-ocular hemorrhage.

CASE 6.—H. A., aged 84, a white man, three weeks previously had had an intra-ocular hemorrhage into the vitreous and aqueous with vision reduced to perception of light in the right eye. Tension was 56; there was no red reflex, and hyphemia filled one third of the anterior chamber. On March 14, 1933, epinephrine packs (1:1,000) were used for fifteen minutes under the upper lid, four times a day, after the method of Gradle. No change was seen after two days. On April 7, the tension was 70. Epinephrine bitartrate, 2 per cent, was used, and one-half hour later the tension was 60; forty-five minutes later the tension was 70; two days later it was 56. Epinephrine bitartrate was used again, and after thirty minutes the tension had decreased to 48. Four days later the eye was comfortable, and the tension was 43. Epinephrine was used again, and one week later the tension was 40, the eye being entirely comfortable. The hyphemia was unchanged. A week later the tension was 41, and the patient was comfortable. Two weeks after this the tension was 48, and on May 10, it was still 48.

By the use of epinephrine, it had been possible to get some reduction of tension, and the patient had been relieved of pain.

This brings me to the last group and the only one in which these drugs appear to have a definite value. They are not often substitutes for operation, but there are always cases in which surgical intervention is inadvisable; the reason for this may be old age, ill health, disinclination of the patient or apprehension of the surgeon because of a greatly restricted field of vision in an only remaining eye. For these, the great advantage of being able to maintain the tension at a low normal with little if any help from miotics, which often in these cases will not, even in irritating strength, keep the tension down to normal, is of vital importance. It is significant also that miotics which have lost their effectiveness often have this restored when they are used in conjunction with epinephrine. A few cases of the action in chronic simple glaucoma will be cited as illustrating how epinephrine acts in the type of case to which, in my opinion, it is best suited.

The following case illustrates the good effect on an eye previously somewhat ineffectually operated on for chronic simple glaucoma.

CASE 7.—W. B., aged 70, a white man, was blind in the left eye from glaucoma. In the right eye the field was reduced to 20 degrees. The patient had been seen

12. Vannas, cited by Peters.[2]

by me one year before, and two years previously Dr. Ewing had performed an iridectomy, after which the tension remained from 30 to 40 for one and one-half years under strong miotics. The patient refused further operative procedures. The field slowly contracted to about 10 degrees, and vision decreased to 10/150. Epinephrine bitartrate and pilocarpine in reduced strength were prescribed, epinephrine being used every four days. Under this treatment, the tension has been maintained at about 17 for the past three months.

In this case, after operation, epinephrine helped to keep the eye at normal tension instead of from 10 to 20 degrees higher.

Case 8.—Mr. B. F., aged 75, had a chronic simple glaucoma that had developed six years previously. Vision was 20/15. For four years he had been treated with miotics, but the tension could not be reduced below 40, even with strong solutions used frequently. An Elliot trephining operation was performed on the left eye, which was followed by detachment of the retina. In view of the patient's age and the operative failure in the left eye, it was thought best not to operate on the right eye. The visual field was markedly constricted, and there was an annular scotoma. On July 2, 1930, vision was 20/15 and the tension, 43. Laevoglaukosan was instilled five times at intervals of fifteen minutes, immediately after which the tension was 43; fifteen minutes later it was again 43, and one and one-half hours later it was still 43. Next day, however, the tension was down to 18. On July 16, it was 28; on July 29, 26 and on August 19, 36. Epinephrine was not used again until March, 1932. The tension during the interval of twenty-two months had ranged from 28 to 40, usually nearer the latter, under strong miotics. Epinephrine bitartrate, 1 per cent, was instilled once on March 8, and within twenty minutes the pupil had dilated 3 mm. The tension which had been 28 just prior to treatment was lowered to 16 two days later. Epinephrine bitartrate was used by the patient every fourth day, for one year, when he died. During this time the tension was taken every second or third week, and it never rose above 17. The field remained practically unchanged during this period, and the vision was 20/15 shortly before his death.

Case 9.—Mrs. E. N., aged 53, a patient of Dr. M. H. Post, had chronic simple glaucoma which she first noticed in September, 1932, but which probably had existed for some time previously. Vision in each eye was 20/15, and the fields were slightly constricted. Tension on October 27 was 31 in the right eye and 55 in the left eye. One instillation of epinephrine bitartrate was made into the left eye, after which the tension in that eye was 33; on October 29, the tension was 24. The eye, previously uncomfortable, was now much easier than it had been for a long time, during which the usual miotics had been given. On November 5, the tension was 19; on November 14, after another instillation of epinephrine bitartrate, the tension was reduced to 15. This slowly increased until on November 30 it was 43. Epinephrine bitartrate was instilled again on that date. On December 7, the tension was 31, and on December 12, 22. It rose slowly to 26, and again an instillation of epinephrine bitartrate lowered it. This case demonstrates the possibility of holding tension down with epinephrine, but in view of the youth of the patient and of the absence of contraindications to operation, a filtration operation was performed on Jan. 13, 1933.

Case 10.—Mr. A. J. W., aged 72, a patient of my associate, Dr. W. E. Shahan, had chronic simple glaucoma. On Nov. 16, 1929, tension in the right eye was 39 and in the left eye, 43. Glaukosan was instilled four times, and the tension

was greatly reduced. It was used again on December 8, three instillations being given, and one week later the tension was 17. Another application somewhat later had the same effect. By this time the patient had consented to operation, which was then performed.

CASE 11.—Mrs. E. C., aged 71, had been under observation for refraction several times in previous years. On Feb. 20, 1928, Dr. Ewing, whose patient she then was, saw a small amount of cupping of the left disk. Vision in the right eye was 20/15, and in the left eye, 20/19. Pilocarpine therapy was given until February, 1930, at which time vision in the right eye was 20/19 and tension, 36; vision in the left eye was 20/120, and tension, 33. At this time the patient came under my care. On March 4 the right eye showed a slight cupping of the disk; the left eye, marked cupping and pallor. The tension was poorly controlled with miotics. Vision failed steadily until the patient was operated on (Elliot trephining) in May, 1930, when vision was 8/150 (eccentric). Operation reduced the tension in the left eye to 18, and it has remained down (between 10 and 15) to date, June 26, 1933, but without improvement in vision. The patient's physical condition is extremely poor. In the right eye the tension could not be kept below 24 with strong miotics. On March 1, 1932, it was 26, and a 1 per cent solution of epinephrine bitartrate was administered. A dustlike haze of the epithelium followed its use; the pupil dilated well, and evenly. Vision on this date was 20/24. On the second day, the tension was 15. Since then the patient has used epinephrine at home every tenth day, together with a 1 per cent solution of pilocarpine, three times a day. For the past year and a quarter, the tension has remained between 15 and 20, under mild miotics. There has been no loss of field or vision. This, like case 3, is an example of maintenance of lowered tension with less miotic in a patient unsuited to operation.

CONCLUSION

I agree with others that laevo-glaukosan and epinephrine bitartrate (about which little has been written, but which acts in a similar manner and is simple to handle and cheaper) are important aids in the non-operative treatment of chronic simple glaucoma, of little value in secondary glaucoma and of no value in acute glaucoma.

BLINDNESS AND PAPILLEDEMA IN GUERNSEY CALVES

A SECOND COMMUNICATION

G. E. DE SCHWEINITZ, M.D.
AND
PERCE DE LONG, M.D.
PHILADELPHIA

In a previous communication [1] about blindness in Guernsey calves, one of us (the senior author) reviewed the literature of this subject, discussed the clinical symptoms of the disorder and recorded the results of an investigation of its pathologic histology.

The chief facts and observations developed by this study, briefly summarized, are as follows: A disease which may be regarded as a clinical entity, well known to veterinarians and others concerned with the care of cattle, but to which comparatively few publications have been devoted, apparently first carefully described from the general and pathologic standpoints thirty years ago by Nettleship and Hudson, characterized by complete blindness and papilledema (choked disk) and practically unassociated with other symptoms, exists among calves (male and female), usually, if not exclusively, of the Guernsey breed, and is generally detected within the first year of life, but may be present at birth.

The important pathologic lesions revealed by this research were: enlargement of the optic disk, depending on marked increase of its neuroglia and swelling of the cell bodies; atrophy of its nerve elements and of those of the optic nerve, the optic tracts and the chiasm; marked degeneration of the retinal ganglion cells, and no gross intracranial lesions but definite edema of the cerebral hemispheres.

As to etiologic factors, food poisoning was excluded, and the opinion was expressed that inbreeding should be regarded as an important predisposing factor in the development of this form of bovine blindness.

The present communication is concerned with the investigation of another blind Guernsey calf, a record of the results obtained and a comparison of these results with those secured and reported in the essay which has been summarized in the preceding paragraphs.

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1. de Schweinitz, G. E.: Blindness and Papilledema in Guernsey Calves, Usually Bulls, Arch. Ophth. **7**:1 (Jan.) 1932; Tr. Am. Ophth. Soc. **29**:321, 1931.

REPORT OF A CASE

History.—A female Guernsey calf, yellowish-brown, a member of the famous Langwater family, was admitted, totally blind, on May 4, 1931, the fourth day after its birth, to the Hospital of the Veterinary Department of the University of Pennsylvania.

General symptoms were lacking, except for a moderate degree of "scours," which yielded promptly to treatment.

The animal was born blind according to the record at the hospital, but the manager of the herd from which the calf came stated he had not definitely detected the blindness until the third day after birth.

Ocular Examination.—This was made by one of us (the senior author) and by Dr. Clarence J. Marshall of the veterinary department of the University of Pennsylvania on the fifth day after the animal was born.

Both pupils were widely dilated, and the irides absolutely unresponsive to strong light flashed into the eyes. The media were clear; there were no ophthalmoscopically visible lesions in the choroid, retina or tapetum.

Papilledema in the sense of a definite elevation of the disk was not present, but over the center of each nerve head a layer of finely spun, pinkish-gray material extended slightly beyond the margins of the nerve heads. This layer was semitranslucent. It did not obscure the emergence and entrance of the principal arteries and veins. The veins, compared with those of a normal animal, appeared to be unusually large.

We had not previously observed an exactly similar condition in any of the other blind calves we had examined and, although not quite sure of its interpretation, regarded it as one which represented an early stage of papilledema.

The animal developed naturally and appeared, except for the blindness, to be normal in all respects. At the end of a month the nerve heads were practically unchanged. Nearly three weeks later (June 23) a slight prominence of the disks was noted, and the material previously described which covered them had taken on a moderate yellowish tint, but had not quite lost its translucency; otherwise there were no lesions.

Autopsy.—The animal was chloroformed and autopsy was performed in our presence on June 23, by Dr. E. L. Stubbs, professor of veterinary pathology, and Dr. M. A. Emmerson, assistant professor of veterinary surgery and obstetrics at the School of Veterinary Medicine of the University of Pennsylvania.

The animal, 7 weeks old, weighed 65 pounds (29.5 Kg.) and appeared to be in good condition. A swelling which had been noted over the third premolar proved to be due to an infection at the root of the tooth, associated with some softening of the surrounding bony tissue. The fluid in this area, in addition to numerous pus cells, contained many of the usual bacteria and some microorganisms which resembled Bacillus necrophorus; there was no actinomycosis.

Gross Morbid Anatomy.—Brain and Skull: The brain and meninges showed no signs of superficial inflammation. The brain and cerebellum, subsequently examined after preservation in a dilute solution of formaldehyde, U. S. P. (1:10), revealed no gross lesions, no tumor, abscess or area of softening.

Nothing abnormal was found in the bones of the orbit, the bony optic canal or the sphenoid or ethmoid bones, or at any other point at the base of the skull. Particular care was accorded to this part of the investigation because Crocker, in one of the animals he had described, reported rachitic deformation of the sphenoid bone and stenosis of the optic foramen.[2]

2. Crocker, W. T.: Cornell Veterinarian **9**:171, 1929.

Lungs: All portions of the lungs seemed to be normal. There were no areas of atelectasis. The pleura was normal in appearance. There was no fluid in the pleural cavities.

Abdomen: Neither the four stomachs nor the intestines revealed the presence of any parasites. The liver (weight, 22½ pounds [10.25 Kg.]), spleen, kidneys, pancreas and mesenteric glands showed no evidence of disease. Specimens from

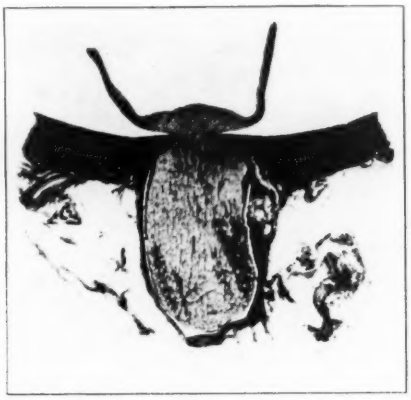

Fig. 1.—Longitudinal section of the nerve head of a blind bull calf showing papilledema (choked disk) and almost complete atrophy of the optic nerve fibers. Weigert stain. This illustration and figures 2, 4, 5, 7, 9, 12 and 13 appeared in the Archives of Ophthalmology (**7**:1 [Jan.] 1932).

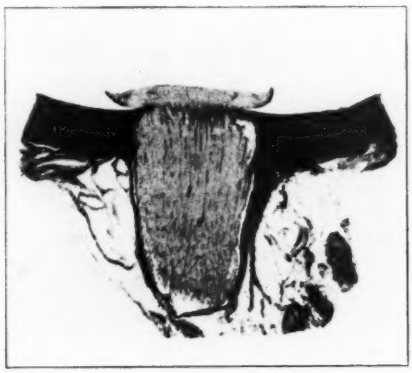

Fig. 2.—Another longitudinal section of the nerve head of a blind bull calf.

these structures were taken for microscopic investigation and placed in a dilute solution of formaldehyde, U. S. P. (1:10).

Eyes, Optic Nerves, Optic Tracts and Chiasm: Both eyes with attached optic nerves, tracts and chiasm were removed intact. There was no distention of the sheaths (hydrops), and not the slightest evidence in any portion of the optic nerves of any block of fibrous tissue or any area of contraction, such as has been described by Allen, T. C. Summers Delez and Crocker.[1]

Microscopic Examinations.—Lungs: The bronchioles and peribronchial tissue contained an exudation with numerous polymorphonuclear and mononuclear cells. A slight edema of the outer side of the alveoli was present. In other words, the lesions resembled those found in the lungs of the bull calf previously described.

Liver: The walls were well outlined; the cell nuclei were distinct, and no pathologic changes were detected.

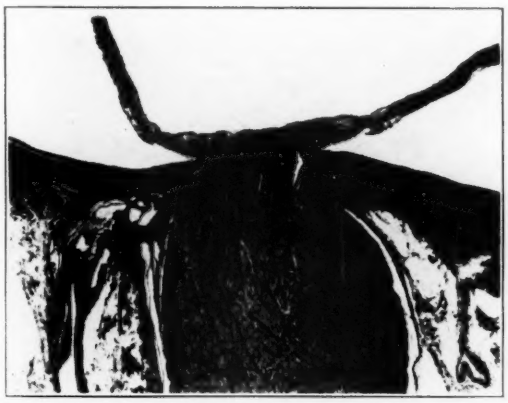

Fig. 3.—Longitudinal section of the nerve head of the blind female calf showing papilledema (choked disk). Compare with figures 1 and 2.

Fig. 4.—Longitudinal section of the nerve head of a normal bull calf. Weigert's stain. Compare with figures 1, 2 and 3.

Spleen, Kidneys and Lymph Nodes: These structures revealed no evidence of pathologic change. Investigation of the muscle tissue taken from the pectoral region failed to indicate any parasites. Its structure was normal.

The stomach, intestines, pancreas and suprarenals, as they had yielded no sign of disease at the autopsy, were not examined microscopically.

Right Optic Nerve: The nerve head was swollen and projected inward. The lamina cribrosa was pushed forward. The swelling of the disk, marked anteriorly, was chiefly evidenced by its projection over the scleral edges. Edema was present. The edematous spaces, however, were small; they contained no coagula (figs. 1, 2, 3 and 4).

Few nerve fibers could be detected; the neuroglia, however, was very prominent, and made up the bulk of the nerve structure. There was no alteration in the walls of the blood vessels, but the perivascular spaces were unusually wide.

On the anterior surface of the nerve head, where the swelling was most pronounced, there was also proliferation of the connective tissue, which, together

Fig. 5.—Cross-section of the optic nerve of bull calf; atrophy of the myelinated nerve fibers. Weigert's stain.

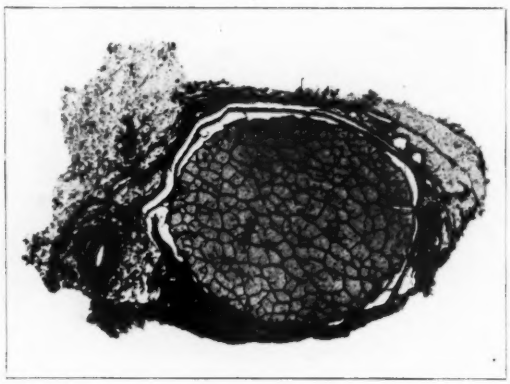

Fig. 6.—Cross-section of the optic nerve of the female calf showing practically complete failure of myelin fibers to accept Weigert's stain. Compare with figure 5.

with the gliosis, may have accounted for the yellowish, somewhat muddy, appearance of the disks noted at the last ophthalmoscopic examination. The retinas were edematous, and the ganglion cells degenerated.

Dr. N. W. Winkelman, professor of neuropathology at the Graduate School of Medicine of the University of Pennsylvania, who examined our slides, submitted a report in which he pointed out that the optic nerves revealed edema manifested

by an increase in the interstitial spaces in addition to a marked gliosis. This decided multiplication of the glia cells was the dominant feature in the usual cellular preparations. The fibroblastic astrocyte was the common glia cell encountered. Phosphotungstic acid stains revealed an intense fibrillar increase. Myelin sheaths were almost completely absent, as was demonstrated by the various modifications of the Weigert stains (figs. 5, 6, 7 and 8).

Left Optic Nerve: The histopathologic changes in this structure in all particulars coincided with those of the right nerve described in the preceding paragraph; possibly the edema was a little more evident.

Fig. 7.—Longitudinal section of the optic nerve of a blind bull calf concerning which a report was previously made, showing a marked increase in macroglial cells.

Optic Tracts and Chiasm: Marked degeneration of the nerve fibers was evident throughout the tracts and was more conspicuous in the regions close to the eye than elsewhere, in this respect corresponding exactly with similar conditions revealed in the optic tracts of the bull calf described in the previous essay. This degeneration of the nerve fibers, as well as the gliosis, constituted the conspicuous feature of the histopathology of both of the optic tracts (figs. 9, 10 and 11).

Brain: Specimens from the cerebral hemispheres prepared for microscopic examination revealed a fairly well marked congestion and an edema manifested by a definite dilatation of the perivascular spaces. Cloudy swelling of the ganglion cells was present. These slides were submitted to Dr. Winkelman, who agreed with this interpretation, and also to Dr. William G. Spiller of the University of Pennsylvania, who studied them in comparison with similar slides from a normal

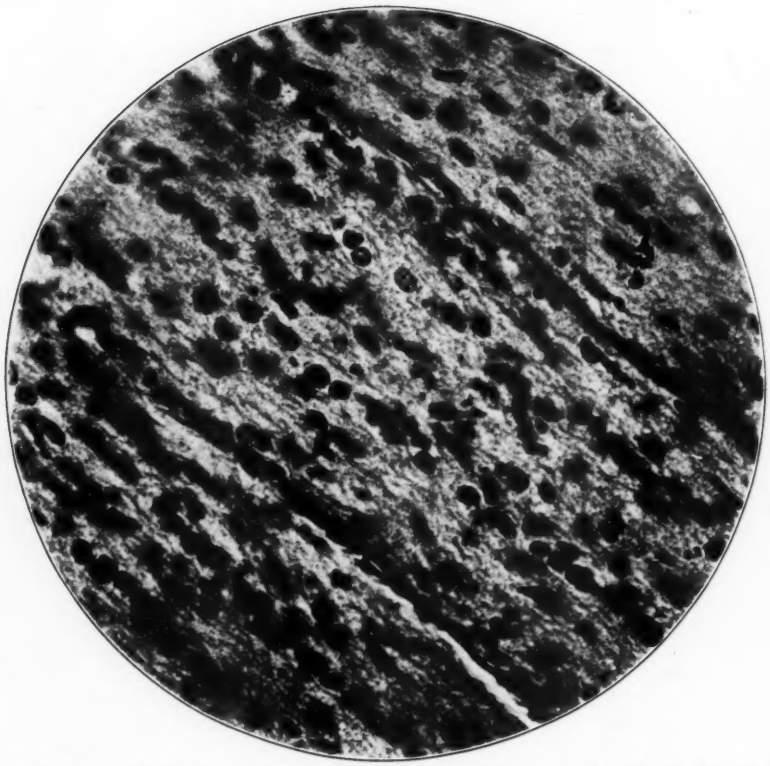

Fig. 8.—Longitudinal section of the optic nerve of the blind female calf showing a marked increase of macroglial cells. Compare with figure 7.

Fig. 9.—Longitudinal section of the optic nerve, chiasm and optic tract of blind bull calf, showing atrophy of the nerve fibers; the atrophy is less marked in the tracts than in the optic nerves.

Fig. 10.—Longitudinal section of the optic nerve chiasm and optic tracts of the female blind calf showing the distribution of the atrophic areas. Compare with figure 9.

Fig. 11.—Longitudinal section of the optic nerve from the female calf showing atrophy and secondary gliosis.

calf (not a Guernsey). He wrote: "The perivascular spaces of His are somewhat larger in the brain tissue of the blind calf than in the normal animal. From this finding an edema of moderate degree may be postulated" (figs. 12, 13, 14 and 15).

Meninges: With the possible exception of a slight fibrosis, no lesions were detected.

Medulla Oblongata: Slight congestion and edema were present, manifested by a dilatation and overfiling of the blood vessels, with a few minute pericapillary

Fig. 12.—Section of a specimen from the right hemisphere of the brain of a normal bull calf taken from an area corresponding with that from which the specimen from the blind bull calf was secured. Pyroxylin (celloidin) embedding; hematoxylin and eosin stain.

hemorrhages, which may have been the result of the method of death and were not regarded as of pathologic importance.

Cerebellum and Spinal Cord: The tissues of these structures were entirely normal.

Summary.—Briefly, therefore, the lesions of the nerve heads, optic nerves, optic tracts, chiasm and cerebral hemispheres corresponded closely with those in the same tissues of the bull calf described in the previous essay, as may readily be seen by comparing the photomicrographs with which this paper is illustrated (figs. 1 to 15).

FREQUENCY, BREEDS AFFECTED, SEX AND ONSET OF BLINDNESS

That this variety of bovine blindess is far more prevalent than the rather scanty literature indicates, as was originally pointed out by Nettleship and Hudson,[3] has been confirmed by the studies of one of us (the senior author) and Dr. Clarence J. Marshall recorded in the previous essay. Indeed, according to investigations carried out with the aid of Dr. G. A. Dick, dean of the school of Veterinary Medicine of the Uni-

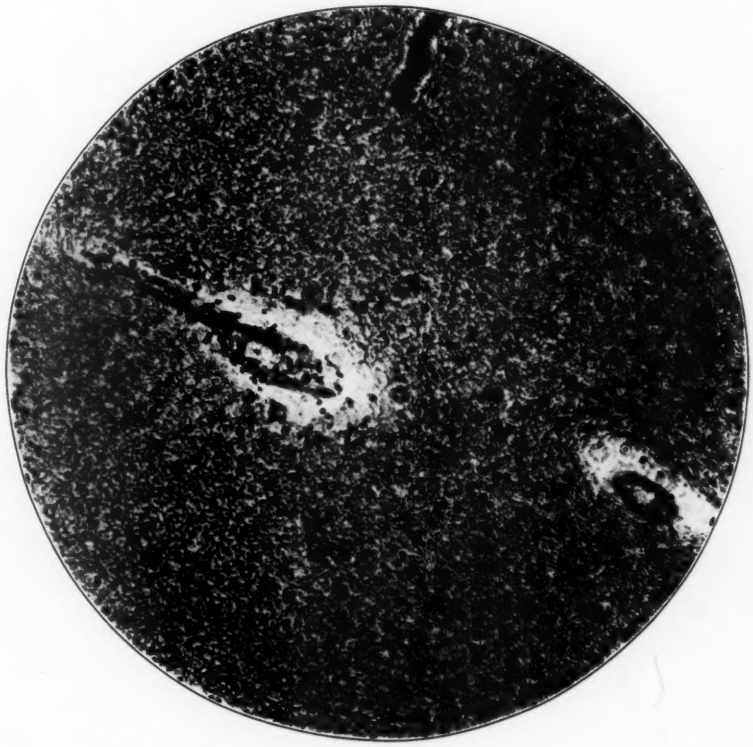

Fig. 13.—Section of a specimen from the right hemisphere of a blind bull calf concerning which a report was previously made, indicating perivascular edema. Pyroxylin embedding; hematoxylin and eosin stain. Compare with figure 12.

versity of Pennsylvania during the last two years, it is evident that the distribution of this disease is widespread in the United States. But it is also true that in certain individual observations this type of blindness may be an uncommon event. Thus, Mr. J. S. Clark of Huntington, L. I., wrote: "At Mixter Farm, where we bred some 4,000 registered Guernseys, I can recall but two animals that were blind in over fifteen years of experience in breeding." [4]

3. Nettleship, E., and Hudson, A. C.: Roy. London Ophth. Hosp. Rep. **19**: 14, 1913.

4. Clark, J. S.: Personal communication to Dr. Dick.

All of the animals, the subjects of this form of blindness that we and the members of the staff of the veterinary department of the University have examined, were of the Guernsey breed, or had a definite Guernsey strain. This fact, of course, does not prove that this condition may not occur in other breeds, but certainly indicates that if it ever occurs it must be very uncommon. Recently we have received from Dr. C. W. Rippon an account of twin Jersey bull calves with blindness,

Fig. 14.—Section taken from the right hemisphere of a brain of the female calf corresponding with section in figure 13, showing perivascular edema. This photomicrograph represents a higher magnification than figure 15. Hematoxylin-eosin stain.

probably of this type. Further reference to these calves appears in a later portion of this essay.

When Nettleship and Hudson published their essay on this subject, they wrote: "We do not know to what extent the disease . . . is confined to males." We are now aware that female calves are by no means immune; indeed, one veterinarian, in charge of a herd of Guernseys, expressed the opinion that the disease was about equally divided among males and females. Whether this proportion obtains throughout other herds in this country, we do not know.

In the previously published communication concerned with this form of blindness, it was stated that the loss of sight usually had appeared within the first year of life. In one animal in the Nettleship-Hudson list, the visual defect was detected when the calf was 2 years of age.

W. J. Crocker, recording an experience in 1919, was the first investigator to point out that some of the calves are born blind or become blind within a few days after birth.

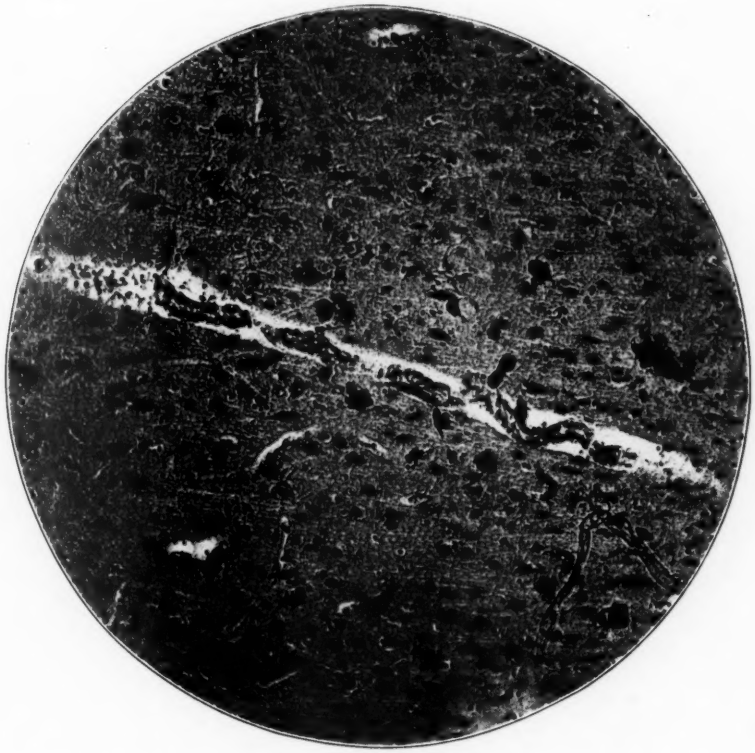

Fig. 15.—Lower magnification of section shown in figure 14.

One of us (the senior author), in 1931, expressed the belief that, although the onset of the blindness in most of the cases appeared to have been sudden, this sudden loss of sight should be regarded as the final stage of visual degradation caused by a process which had been gradually developing for a considerable period of time and which may have begun in prenatal life. A similar opinion was originally recorded by Nettleship and Hudson.

That such was the case in the female calf on which this essay is based, there is no doubt. It is manifestly impossible that the widespread degeneration could have developed in the three days prior to the detection of the blindness; it must have been elaborated in prenatal life.

VARIATIONS IN THE OPHTHALMOSCOPIC PICTURE OF THE BLIND CALVES

It appears that there are two types of ophthalmoscopic pictures: 1. Papilledema and its later stages, that is, the type in which the process has been long continued, with no other symptoms.

This was the case in all of the blind calves we have studied. Nettleship and Hudson stated that in the animals they examined ophthalmoscopically, no definite changes were noted in the nerve head, and yet in one of them, investigated microscopically, "optic neuritis was found." It would seem that these authors did not themselves make the ophthalmoscopic examinations.

2. Papilledema associated with hemorrhage and chorioretinitis. This association has been described by MacCallan and Mann,[5] by Summers [6] and also by Dr. Lewis B. Porter of Providence, R. I., in a 6 months old Guernsey bull calf with blindness and choked disk.[7]

The ophthalmoscopic appearance of the nerve heads of these blind animals apparently present themselves in three stages:

1. First, the optic disks are covered with a finely spun layer of pinkish-gray material which extends beyond their margins. There is no elevation of the nerve heads. At the end of about two months a slight prominence begins to appear. This statement is based on the examination of the female calf described in this paper, and is referred to in an earlier portion of the essay.

2. After about from six to eleven months, a definite choked disk (from 3 to 3.5 D.) may be evident. This statement is based on a personal experience with eight animals.

But, naturally, it would be impossible to maintain that this period must elapse before a choked disk, from 3 to 3.5 D. of swelling, appears. It may be present at an earlier date; it may take a longer time for the elevation of the disk to develop, or it may not at all be ophthalmoscopically indicated, although microscopic examination reveals optic neuritis (Nettleship and Hudson). It represents merely a suggestion as to the possible course of events.

3. After a long time, how long is not known, well marked atrophy of the optic nerve, ophthalmoscopically revealed, is present; the edema has subsided, and the nerve heads are flat and grayish white. There is no noticeable diminution in the size of the blood vessels, except that the veins are smaller in caliber than those of a normal animal.

The chance to investigate the eyegrounds of mature animals with this form of blindness must be an unusual one because usually, if not

5. MacCallan, A. F., and Mann, Ida: Tr. Ophth. Soc. U. Kingdom **46**:229, 1926.

6. Summers, T. C.: Tr. Ophth. Soc. U. Kingdom **47**:221, 1927.

7. Porter, L. B.: Personal communication to the authors.

always, they are killed as soon as the visual loss is detected, that is, within the first year of life. Hence, the following experience is recorded:

Visiting two herds of Guernseys in Maryland, about 2 miles apart, Dr. Dick and one of us (the senior author) found in one a cow, 4 years old, which had been born blind, and in the other a bull, also 4 years of age, blind since the eighth month of life. In all other respects the animals were in excellent condition.

In each instance the ophthalmoscope revealed advanced atrophy of the optic nerve, the appearance of the nerve heads corresponding exactly with those described in a preceding paragraph (no. 3), on which, indeed, it is based. For comparison, the fundi of several normal animals were examined, and we satisfied ourselves that our observation was correct.

PROGENY OF THE BLIND ANIMALS

So far as we are aware, this form of blindness is not transmitted to the offspring of the blind animals, sires or dams. The progeny of two of the bulls in the pedigree recorded by Nettleship and Hudson were normal.

The two 4 year old animals, a bull and a cow, studied by Dr. Dick and one of us (the senior author) in two Maryland herds of Guernseys, previously referred to, had several times respectively been responsible for normal offspring. Similar confirmatory evidence has been obtained from various veterinarians. But in all of these instances one of the mated animals, sire or dam, was normal, and thus far we have been unable personally to ascertain whether the progeny of two blind animals would be born blind, or become blind during the first year of life, that is, inherit this disease.

Somewhat in this connection it seems appropriate to include a report, sent to us by Dr. L. G. Redding of Scranton, Pa., after a visit he paid to a farm where there was a herd of Jersey cattle, and where he discussed with Dr. Rippon, the veterinarian in charge, the type of blindness to which this essay is devoted, and requested him to write the record which follows:

> About the year 1922 a famous bull called "The Cid," the son of "Castile II" and "Sea Lad," was purchased in the island of Jersey when 1 year old. At the time he was imported to America, he was 7 years of age.
>
> "The Cid" was mated to choice daughters of "Oxford You'll Do," "Combination Premier," You'll Do's Victor" and a few others including "Sultana's Golden Jolly"—all of them famous sires. In all this breeding nothing happened except that a mating between "The Cid" and a daughter of "Oxford You'll Do" produced a beautiful pair of bull calves (twins) that were cared for, as were the other calves, in modern fashion. Nothing unusual was noticed in them. They ate, drank, played and seemed to enjoy themselves in the same manner as other calves, but were always kept together, and no other calves mingled with them.

At about 5 months of age they were sold and were to be sent to a ranch in Texas. As a veterinary investigation was necessary prior to their shipment, and also as a guarantee to the purchaser that they were sound, a veterinarian was called to examine them. He found them to be in perfect health, perfectly formed, but as blind as could be. No pathologic conditions were found except that the direct light reflex of the pupils, widely dilated, was absent. As the veterinarian could find no other cause for this condition, he called it "congenital." As a result of this condition the animals were not shipped to Texas, but were given to friends in Pennsylvania to be used because of the valuable breeding. Although in the opinion of the owner of the calves and of the veterinarian the blindness would not in all probability be transmitted, the practice of line breeding or inbreeding was forbidden. After seven years of breeding it was found that neither of these bulls had ever sired a blind animal.

However, accidentally, a daughter of one of these bulls was bred to a son of the same bull, that is, to a half brother, and this produced a male calf which was blind and was immediately killed. Unfortunately, these animals were not in circumstances where a real series of experiments could be undertaken.

So this case evidently represents a recessive condition and appeared only when two "recessives" were bred to each other.

Apparently the blindness of the twin bull calves, which were Jerseys, was like that which we have heretofore found only in animals of the Guernsey breed. It is a fact, however, that the original root stock of Jerseys and Guernseys is closely similar, if not identical.

So far as we understand this matter, neither the daughter nor the son of one of the blind bulls which Dr. Rippon describes was blind, although the mating produced a blind male calf. In other words, we have yet to ascertain what the ocular condition of the progeny would be when both sire and dam are blind. That blindness would result is possible, and if so it would indicate that the disease is inheritable.

SOME COMMENTS ON THE HISTOPATHOLOGY OF THIS DISEASE

The outstanding lesions in the optic nerve apparatus, from the optic disks to and including the chiasm, have been recorded in detail, being, in brief, edema, degeneration of the nerve fibers and gliosis associated with moderate edema and congestion of the cerebral hemisphere, not found elsewhere in the brain tissue.

It is interesting to note that the lesions in the tissues of the female calf, almost certainly born blind, with which this essay is chiefly concerned, were just as pronounced—if anything, more pronounced—at the end of seven weeks as those in the animals whose blindness was not detected until well nigh a year (from eight to eleven months) had elapsed since their birth.

This fact would seem to support the opinion that the morbid process was present or beginning to develop during the earliest period of prenatal life.

Examination of figure 6 shows that in the cross-section of the optic nerve depicted, myelinated fibers are absent, no trace of the Weigert stain being visible. Now, according to Ida Mann [8] the exact time at which the fibers become medullated in the human embryo has not been decided. This author quoted C. W. Sattler who stated that "in a human embryo there was no medullation at all at five months, but in a 7 months' foetus medullary sheaths could be traced from the optic tract to the beginning of the optic nerve and by term these had reached the lamina cribrosa."

Whether this condition obtains at the same time with embryos of calves, we have not been able to ascertain. But it is probable that it does, and if so the apparent absence of medullations as indicated by Weigert

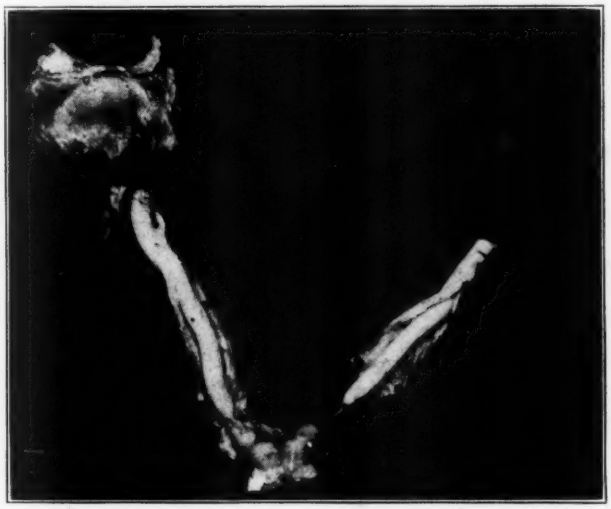

Fig. 16.—Photograph of optic nerves of a 6 month old blind Guernsey bull calf with papilledema from Aldrich Farm, Rohoboth, Mass., showing interruption of the continuity of the optic nerves by fibrous blocks (courtesy of Dr. L. B. Porter, Providence, R. I.).

stains may in part be explained by failure of development and not by degeneration.[9]

The influence of pressure on, or constriction of, the optic nerves in the development of this form of bovine blindness has been referred to by several authors.

The late Dr. Reginald Allen found a constriction at one place in the optic nerve and at this point a spot of softening to which the sheath

8. Mann, Ida: The Development of the Human Eye, Cambridge, Mass., Harvard University Press, 1928, p. 140.

9. The suggestion that failure of development of medullary fibers should be considered comes from Dr. Jonas Friedenwald.

was adherent. Crocker noted "stenosis of the optic foramen or canal . . . and pressure atrophy," and T. C. Summers observed a "block of fibrous tissue in the nerve." In these instances apparently only one nerve was examined.[10]

For a perfect demonstration of constriction in the optic nerve in some of these animals, we are indebted to Dr. Lewis B. Porter of Providence, R. I.; this was communicated to us in a letter which he permits us to utilize.

He examined a 6 month old Guernsey male calf, completely blind, with choked disks, elevated 2 D., and widely dilated pupils unresponsive to light. A complete autopsy was performed, and a constriction distal to the chiasm was found in each nerve. In the right nerve the separation was complete and in the left one nearly so. The brain has not yet been studied microscopically. The reproduction of a photograph which Dr. Porter permits us to publish illustrates well the conditions which were present (fig. 16).

Dr. Verhoeff examined these nerves and wrote to Dr. Porter as follows:

> Sections showing the constriction in the optic nerve prove that the constrictions are not artefacts, but sharply defined lesions in optic nerves. The nerve fibers have been completely destroyed in the constricted portions. This is certainly adequate cause for the blindness, but I am at present utterly unable to explain such a lesion in the optic nerves.

Evidently, therefore, in some of these cases constrictions or blocks are present in the optic nerves. Equally, it is a fact that such is not always the case in that in two of these animals we have studied investigation failed to disclose any evidence of their presence.

Dr. Verhoeff has suggested that by a careful examination of serial sections of the optic nerves of the blind animals we have examined, a spot or area might be found with lesions representing the earliest indication of the formation of such constrictions or fibrous blocks not otherwise detectable. None of our numerous slides, taken from various portions of the optic nerve of the female calf, with which this paper is concerned, admittedly not including every part of the nerve, gave any indication of such a condition; only atrophy of the nerve fibers, that is, degeneration of the myelin fibers, was seen, and the animal was totally blind. Therefore in this calf a formed block of fibrous tissue was certainly not the cause of blindness, and it seems unlikely that a very early stage of such a condition was present.

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10. Delez (J. Am. Vet. A. **74**:222, 1929), experimenting with certain foodstuffs in producing blindness in cattle (calves from birth to 2 years), found in the optic nerve of one of them a marked contraction (3 mm. long and 1.5 mm. wide) with atrophy of the fibers at the point of constriction.

In the animals with this form of bovine blindness which we have examined, the ophthalmoscope has revealed papilledema in different periods of development as is definitely portrayed in the photomicrographs (figs. 1, 2 and 3).

As the microscopic examination of the edematous nerve heads failed to reveal any evidence of past or present inflammation, obviously the cause of such edema of the disk should be attributed to an increase in intracanial pressure, which Dr. Verhoeff, who examined the slides prepared from the optic nerve apparatus of the blind bull calf described in the former communication, thought had not been of high degree but of long duration.[11]

Careful expert study of the sections of the cerebral hemispheres of the female calf recorded in an earlier portion of this essay, and also of those of the bull calf described in the former communication, demonstrated the presence of definite edema and therefore an agency for creating the increased intracranial pressure responsible for the papilledema.[12]

CONCERNING THE ONSET OF THE BLINDNESS

Although the onset of the blindness in most of the cases thus far reported was sudden, or suddenly noticed, this sudden blindness might well have been, as Nettleship originally pointed out, the final stage of the usual degeneration created by a process which had been gradually developing for a considerable period of time.

The lesions of the optic nerve apparatus of the female to which this communication is devoted certainly appeared before the animal was born and were present a few days after birth.

It seems most likely that in all of these cases of this form of blindness the origin of the disease should be traced to prenatal life. There it may attain its full development, and the animals are born blind; or the process may be a gradual one, and its final stages may not be reached until a number of months have elapsed.

CONCERNING POSSIBLE ETIOLOGIC FACTORS

Efforts to discover the cause of this variety of blindness have been made by most of the physicians and veterinarians who have studied the subject.

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11. Dr. Verhoeff, in this connection, has also stated: "the possibility, however, that the papilledema was due to a pre-existent slight inflammation of the nerve with marked edema, is not positively excluded."

12. It is proper to state that Dr. Verhoeff, after his examination of the slides from the brain of the bull calf described in the former communication, declared that he was unconvinced that an actual edema was present. He has not had the opportunity of studying the slides from the brain of the female calf.

Nettleship and Hudson suggested that "something wrong in the dietary" should be accused in this respect, but were unable to advance evidence in proof of this theory.

Delez [10] found, among thirty animals with which he experimented on the effects of various food poisonings, two animals with axial degeneration of the optic nerves.

But, so far as we understand the matter, the other conditions revealed did not correspond with those which pertain to the familial type in which we are interested.

It is hardly conceivable, if food poisoning were the etiologic agent, that this factor would not have been discovered by veterinarians and others in charge of herds of Guernsey cattle. In fact, some experiments along this line have been made, for instance, by Crocker, with negative results.

Nettleship and Hudson, because the five bulls in the pedigree they reported were related to each other by blood, advanced the idea that the blindness might be analogous to hereditary atrophy of the optic nerve (Leber's disease), and a similar independent suggestion was made by one of us (the junior author of this essay). This matter should receive further attention.

So far as we now know, inbreeding should be regarded as a potent predisposing factor in the development of this variety of blindness, almost always in animals of the Guernsey breed. It is possible that another contributing factor should be taken into consideration, namely, a congenital inferiority or an abiotrophy of the optic nerve apparatus which caused premature death or decay of its tissues.

Confirmation of the influence of inbreeding has been furnished by Mr. J. S. Clark of Huntington, L. I.,[13] who wrote:

> A friend of mine, some years ago, found a Hollander breeding registered Guernseys in Wisconsin who had ten blind heifers. This man had not purchased any outside bulls for thirty years. He continually bred sire to daughter and as one of the earlier bulls was blind, this affliction became a fixture through inbreeding.

CONCLUSIONS

Observations and studies in this country and elsewhere adduce adequate grounds for the following statements, briefly summarized in repetition: that a form of permanent blindness is not uncommon among pedigree male and female Guernsey calves, otherwise apparently normal; that the ophthalmoscopic signs of this condition are papilledema alone or papilledema associated with patches of choroiditis and occasionally with small hemorrhages; that the histopathology of this disease consists in extensive atrophy of the optic nerves, optic tracts and chiasm; that

13. Clark, J. S.: Personal communication to Dean Dick of the veterinary department of the University of Pennsylvania.

the continuity of the optic nerves may be interrupted by a block of fibrous tissue, but that this feature is not a constant one; that the cerebral hemispheres reveal edema which probably causes the increase of intracranial pressure responsible for the papilledema; that the blindness may be present at birth or may not be detected for a number of months (from eight to eleven), only rarely at a later period; but it is probable that the lesions of this disorder always begin in prenatal life, when, indeed, they may attain a marked development or may not reach their maximum until a number of months after birth; that a blind animal, dam or sire, apparently does not transmit the blindness to its progeny as a "dominant" feature; that thus far the opportunity has not arisen to ascertain whether, if both dam and sire were blind, the blindness would be transmitted to their offspring; that this form of blindness should probably be regarded as a special or familial disease which depends largely on inbreeding for its origin, whereby two "recessives" come in contact.

A number of problems related to this disorder remain unsolved. They are important and deserve additional study from all standpoints.

SCHÜLLER-CHRISTIAN DISEASE (XANTHOMATOSIS)

REPORT OF A CASE WITH POSTMORTEM OBSERVATIONS

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In June, 1930, I brought to the attention of the American Ophthalmological Society the syndrome of "exophthalmos associated with diabetes inspidus and large defects in the bones of the skull," and described the case of a patient who had come under my care. By surgical exploration of the orbit I was able to establish definitely the cause of the exophthalmos by finding xanthomatous nodules in the orbit. It was possible also to explain the impairment of sight by the presence of a firm mass that completely buried the optic nerve. Previously Schüller, Christian and others had assumed that the exophthalmos in their reported cases was caused by large defects in the roof of the orbits. In other words, they thought that the pathologic process had performed decompression, with encroachment of the contents of the cranial cavity on the contents of the orbital cavity. At the time of my exploration of the orbit a part of the optic nerve was removed with the new growth enclosing it. Although several cases of the syndrome had been reported, no surgical entry into the orbit had been made, and the true state of affairs in the orbit had not been known or even guessed. An important additional finding was that, although the bony roof of the orbit was largely absent, the periosteum was intact and in the proper place. The roof offered good resistance to pressure by a finger from within the orbit, and no pulsation could be felt. Presumably the xanthomatous growth had created a substantial layer of tissue above the orbital periosteum and very likely the new tissue was at least in part fibrosed. Thus a reenforcement for the hole in the roof was in effect, so that support for the cranial contents was adequate, and the newly formed partition prohibited transmission of pulsation.

Since my report was published I have again operated on this patient to remove a xanthomatous nodule from behind the right ear, and to explore the orbit again. The new nodule was yellow and rubbery, but the pathologic tissue that nearly filled the orbit was harder than cartilage and firmly adherent to the orbital wall, so that removal of a specimen from behind the eyeball was not easy. The tissue was thoroughly fibrotic and without yellow color. Physically and mentally the child has failed to grow, and his appearance is remarkably similar to that

described in 1930. Probably, widespread fibrosis is in process, and I fear that one day it may be possible to have a necropsy.

Several case reports have been published recently, but I should like to point to another case of well established Schüller-Christian disease, especially because it is possible for me to give the results of a thorough postmortem examination.

REPORT OF A CASE

History.—Alvin Ulrich, a white child, the son of American parents, had been studied at the Englewood (N. J.) Hospital, where he was admitted on May 9, 1931, and discharged on June 7. There, a proper diagnosis was made, and he came under the observation of Dr. G. F. Worcester, who referred him to the eye department of Columbia University for observation and care. He was admitted to Babies Hospital on June 25, 1932, and he died there on July 13. While there, Dr. Katherine K. Merritt supervised his care. Necropsy was performed by Dr. Martha Wollstein, and painstaking laboratory study of the pathologic tissue was made by Dr. Beryl H. Paige. Dr. Merritt and Dr. Paige anticipate publication of their studies of this case in the pediatric literature.

The patient was 3½ years old on admission to Babies Hospital. He was the third child of five healthy children. He was apparently normal until about the end of the first year, when eczema of the head and neck developed. At the same time a sore mouth developed with swollen, bleeding gums and decay and loss of teeth. When he was about 2 years of age slight prominence of the eyes was noticed. This had increased gradually, the right eye being more prominent than the left. During the last few weeks before admission the eyes had been red, with swelling and watering. The members of the family thought that the child had no sight with the right eye, but a little with the left. For some months there had been great thirst, so that the child would drink anything. It was said that he had thrown flowers out of a vase so that he could drink the water from it. For several days he had been especially tired and weak, willing to drink but unwilling to eat.

On admission physical examination was made by Dr. Mary Adams, who made the following notes:

"Temperature, 101.6 F. Pulse, 160. Respiration, 28.

"*General Appearance.*—An undersized, underdeveloped and emaciated white boy of 3 years, cachectic, apathetic and chronically ill. The marked exophthalmos and yellowish pallor are his most striking characteristics.

"*Skin.*—Dry scabs of infected eczematous lesions all over scalp. Impetigo over back and left thorax. Skin pale, yellowish, dry—mucous membranes very poor color.

"*Glands.*—No general glandular enlargement. Epitrochlears, axillaries, inguinals not felt.

"*Head.*—No apparent mastoid tenderness.

"*Eyes.*—Very marked exophthalmos, right eye more than left, with some swelling and ecchymotic discloration of orbital tissues on right. Marked conjunctivitis and keratitis with corneal opacity and purulent discharge in right eye. Left conjunctiva, sclera and cornea clear. Patient has no sight in right eye, but apparently has some perception of objects in left. Eye movements not well performed although there are no definite ocular palsies. Left pupil reacts to light.

"*Nose.*—Slight mucopurulent discharge.

"*Ears.*—Both canals full of soft, yellow flakes of thick, foul-smelling, purulent discharge. When this is cleaned out a pair of dull, corrugated, thick, unhealthy drums are revealed in which no landmarks are to be seen.

"*Mouth.*—All teeth missing except the upper incisors which are loose, sordid and unhealthy. The gums are soft, irregular and retracted. No bleeding.

"*Throat.*—Tonsils pitted, scarred and much enlarged, almost meeting in the midline. Not inflamed.

"*Neck.*—Not remarkable.

"*Thorax.*—Narrow from side to side with marked pigeon breast. Lungs clear to palpation and auscultation. Heart not apparently enlarged, sounds clear, no murmurs, rate very rapid.

"*Abdomen.*—Very full and protuberant—slight dulness in flanks (? small amount of ascites). Liver and spleen both enlarged: the spleen is felt as a large firm mass extending 3 fingerbreadths below the costal margin and somewhat tender. The liver edge is also felt 3 fingerbreadths below the costal margin.

"*Genitalia.*—Normal male, without phimosis. Both testes descended.

"*Extremities.*—Normal contours and movements, except for thinness.

"*Neurology.*—No neck stiffness or Kernig sign. Reflexes in lower extremities all hyperactive with a shortly sustained bilateral ankle clonus. No Babinski sign. Cremasterics and abdominal both very brisk. No exaggeration of reflexes in upper extremities."

Laboratory Report (June 26, 1932).—Examination of the blood showed: hemoglobin, 50 per cent; red cells, 3,880,000; platelets, 184,000; white cells, 3,800; polymorphonuclear leukocytes, 29 per cent; lymphocytes, 70 per cent; monocytes, 1 per cent. There were achromia, marked anisocytosis and poikilocytosis.

The blood chemistry was as follows: nonprotein nitrogen, 36.3 mg. per hundred cubic centimeters; chlorides, 567 mg.; sugar, 97 mg.; calcium, 9.6 mg.; phosphorus, 4.8 mg.; cholesterol, 179 mg.; albumin, 3.49 per cent; globulin, 2.07 per cent; fibrinogen, 0.492 per cent; carbon dioxide combining-power of plasma, 41.6 per cent by volume; direct van den Bergh reaction, negative; indirect reaction, 1 plus.

The specific gravity of the urine was 1.007. Many doubly refractile lipoids were seen.

The reaction to 0.1 and 1 mg. of tuberculin was negative.

A routine Kahn test was negative; a presumptive test was also negative.

Roentgen Report.—Roentgen examination of the entire skeleton, except the vertebral column, showed mutiple sharply demarcated lesions of negative density throughout the bones of the cranium, both scapulae, the ribs, the pelvic bones, both femora and the right humerus.

Although these films were not taken for special detail of the mandible, definite similar defects could be seen involving a large portion of the mandible. A single lesion was seen in the left fibula. The tibiae did not show definite changes.

An anteroposterior view of the chest revealed an extensive patchy increase in density in both pumonary fields with apparent thickening of the pleura along the small interlobar fissure on the right.

Lateral views of the mastoids showed practically no pneumatization. The density of the petrous portions of the temporal bones was marked as compared with the remainder of the skull.

The changes were consistent with the clinical diagnosis of xanthomatosis and indicated a very extensive skeletal involvement and showed involvement of bones that was definitely not of membraneous origin. That is, this case was absolute proof that xanthomatosis involves bones of endochondral origin such as the femora, which were markedly and unquestionably involved. There was also definite roentgen evidence of pulmonary changes which, in the absence of signs of pulmonary infection, probably indicate xanthomatosis of both lungs. This lesion was more marked on the right than on the left.

There were multiple foci of diminished density scattered through the bones of the skull, varying from 1 mm. to 3 cm. in diameter. The largest area was situated in the lower portion of the right frontal bone, where this was contiguous with the greater wing of the sphenoid. The major portion of the latter bone seemed to be markedly involved. The contours of these areas of diminished density were multiform, the borders were fairly sharply demarcated, and both the outer and the inner table and the diploic space were seen to be involved. There was no

Fig. 1.—Photograph of the head of a child, showing lesions of the skin and bilateral exophthalmos, with destructive ulceration of the right cornea.

evidence of generalized widening of the diploic space or of generalized atrophy of the tables as is seen in erythroblastic anemia. On the contrary, the changes were definitely focal. This involvement included all the bones of the vault of the skull, with the greatest concentration in the posterior portion of the frontal and the anterior portion of the parietal bones. The greatest area of destruction appeared to be in the right greater wing of the sphenoid. The body of the sphenoid was also definitely involved, with destruction of the anterior portion of the floor of the sella turcica. Both anterior and posterior clinoid processes were small and blunted. The mandible was also markedly involved, with several large, irregular areas of diminished density in the body of the mandible on the right. Many tooth buds, both temporary and permanent, had been lost. In the frontal views, extensive destruction of the lateral portions of both orbital plates was seen, the right frontal plate being more involved than the left. The right sphenoid ridge also showed marked destruction laterally. The temporal ridges were intact, but numerous areas of diminished density were present in the petrous portion of both temporal bones. Despite these lesions, the general density of the remainder

of the petrous portions indicated a diffuse sclerosis. The mastoids were practically nonpneumatized.

Extensive multiple areas of diminished density were present in both scapulae and in the ilia. The body of the right ischium showed similar multiple areas of diminished density. Both pubic bones were free from involvement.

The only lesion in the upper extremities was a poorly demarcated but definite area of diminished density in the upper third of the right humerus with destruction of the inner aspect of the cortex bordering on this area, particularly posteriorly. Both femora showed multiple small and large areas of diminished density. These could be seen clearly and lay within the medullary cavity, resulting in erosion of

Fig. 2.—Roentgenogram of the skull, showing numerous defects.

the inner surface of the overlying cortex. There were no changes anywhere on the external surface of the cortices to indicate that erosions had taken place primarily from the periosteum. The tibiae were free from lesions. The left fibula showed an area of diminished density in the upper one-sixth, with erosion bilaterally of the cortex from within.

There was a definite increase in the bronchovascular markings and medial zones, with a patchy increase in density in the inner pulmonary fields, not unlike multiple bronchopneumonic consolidations with peribronchial thickening. Two of the ribs showed areas of diminished density similar to those seen in the other long bones.

During the patient's stay in the hospital polyuria and polydipsia were extreme, and no attempt was made to control them by the use of solution of pituitary or other means. He had a fever between 101 and 104 F. The general condition became pro-

Fig. 3.—Section of the femur, showing extensive xanthomatous invasions of the marrow and the bone.

Fig. 4.—Specimen of the parietal bones, including part of the sagittal suture. Defects of the outer table can be seen. These are filled with xanthomatous material.

Fig. 5.—Frontal fossa of the skull; interior of the cranial cavity. Large bony defects are present on the right side. There is reenforcement of the defects by a layer of xanthomatous material about 3 mm. thick.

gressively weaker, and four days after admission a transfusion was given. The eczema spread over the chest and back, and five days after admission a petechial eruption broke out over the lower part of the abdomen and the legs. The liver grew larger. The hemoglobin dropped in one week from 62 to 33 per cent, and there was a marked drop in the platelets. The petechial eruption spread over the whole body. He had three high voltage roentgen exposures of the head. On July 8 he had a second transfusion, but on July 13, three weeks after admission, he died.

During the patient's stay in the hospital the left cornea was not sufficiently exposed to become ulcerated. The cornea of the right eye was subjected to continuous exposure which called for suturing of the margins of the lids and the formation of adhesions, but the physical condition of the patient was so bad that even a minor operative procedure was thought inadvisable. The cornea and protruding conjunctiva were kept anointed, and part of the time were covered by a protective dressing. On the sixth day the cornea of the right eye perforated, and necrosis of the iris developed.

Necropsy Observations.—The necropsy was performed seven hours after death.

The anatomic diagnosis was: generalized xanthomatosis of the bones, dura mater, hypophysis, infundibulum, periosteum, orbits, skin, thymus, pleura, lungs, heart, peritoneum, spleen, liver, pancreas, lymph glands and retroperitoneal adipose tissue; splenomegaly; fatty liver; ascites; subcutaneous edema.

The body was that of a 3 year old white male child. The scalp was scaling and crusted. Over the face, body and lower extremities were innumerable petechiae, and on the thorax were groups of small hemorrhagic scabs and crusts. There was marked exophthalmos of both eyes. The abdomen was distended, and the hands and feet were edematous.

The peritoneal cavity contained less than 100 cc. of fluid. The spleen and liver were large.

Each pleural cavity contained a few cubic centimeters of clear fluid.

The site of the thymus was occupied by a mass of firm bright yellow tissue, measuring 3 cm. in width and 4.5 cm. in length. This mass was firmly adherent to the pleura, covering the medial surfaces of the upper lobes of both lungs, and to the posterior surface of the sternum. On section no thymic tissue could be identified.

The heart was of normal size. On the surface of the right auricular appendage were several small orange-colored plaques. The valves were normal, except for an atheromatous patch in the aortic leaflet of the mitral valve. There was no hypertrophy of the myocardium.

Just above the sinuses of Valsalva were tiny atheromatous streaks and flecks.

The thyroid gland was normal.

The larynx, trachea and main bronchi were normal.

The pleura of both lungs was diffusely and irregulary thickened, varying in color from pale gray to yellowish gray. On section the pleura in many regions reached 1 mm. in thickness. At the site of attachment to the thymic mass xanthomatous tissue extended into the parenchyma of the lung for 3 mm. In the lower lobes of both lungs an extensive increase in connective tissue produced irregular anastomosing bands and nodules from 2 to 5 mm. in diameter. A lesser degree of fibrosis occurred in the upper lobes. The lymph glands at the hili of the lungs were small.

The spleen weighed 340 Gm. It was purplish red and moderately firm. The capsule was tense. On the posterior margin of the organ and extending upward onto the diaphragmatic surface lay a plaque of yellowish-gray tissue, 3 cm. in its greatest width and about 1 mm. thick. On section the cut surface of the spleen was purplish red; the malpighian bodies were small.

The liver weighed 910 Gm. The cut surface was bright yellow, and the lobular markings were distinct.

The gallbladder was normal.

The pancreas was normal. The lymph glands about its head were large, the largest measuring 1.5 cm. in length. Externally and on section multiple punctate hemorrhages were found. The nodes along the body and tail of the pancreas measured from 2 to 5 mm. in width and were deep red.

The gastro-intestinal tract was normal. The mesenteric glands measured up to 12 mm. in size and were pale red.

The suprarenal glands weighed 10 Gm. Their cortices were less than 1 mm. thick and were ochre yellow.

The kidneys weighed 112 Gm. Except for pallor they were normal. In the peripelvic adipose tissue lay small orange-yellow masses, about 3 mm. in width.

The ureters, bladder and testes were normal.

The marrow of the diaphysis of the left femur was deep red, mottled with irregular bright yellow and yellowish-gray masses, sufficiently large in places to replace entirely the normal marrow and to invade the cortex, thus producing irregular "moth-eaten" erosions of the inner half of the cortical bone (fig. 3).

The ninth rib on the left side showed changes similar to those of the femur.

The inner surface of the dura was smooth. In the vicinity of the torcular herophili the dura was thickened by a wedge-shaped mass of firm, bright yellow tissue, 1 cm. wide and 2.5 cm. in length, which surrounded and compressed the sinuses but did not invade them. The sella turcica was filled with elastic, rubbery tissue from the surface of which projected the thickened infundibulum and the fifth cranial nerves. Part of the body of the sphenoid, containing the sella turcica and hypophysis, was removed *en bloc*. On section the pituitary body appeared to be compressed against the dorsum sellae by xanthomatous tissue which surrounded it anteriorly and superiorly. In the segment of sphenoid removed the bone was extensively replaced by a rubbery yellow mass.

Between the dura and the cranial bones were xanthomatous plaques, most extensive over the floor of the middle fossa, where they reached a thickness of from 3 to 4 mm. over the body of the sphenoid bone. When the dura was removed a widespread replacement was seen of the body and greater wings of the sphenoid and the squama of each temporal bone by firm brownish or bright yellow rough tissue. The petrous portions of both temporal bones and the right mastoid showed widespread xanthomatous masses. The squama frontalis lateral to the right orbital plate was eroded on the inner surface and covered by xanthomatous tissue. The cranial surfaces of both orbital plates were intact. Part of the right orbital plate was removed; the bone was thin and brittle, and adherent to its orbital surface was a layer of gray translucent tissue of almost cartilaginous consistence. Beneath it in the orbit was a bright yellow mass.

Multiple small, sharply circumscribed defects were found in the frontal and parietal bones. Many appeared to involve only the outer table of the bones, but several extended through the entire thickness of the skull.

The brain was normal externally and on section, except for the changes described in the hypophysis and infundibulum.

Microscopic Examination.—In the malpighian bodies and splenic pulp there were an extreme depletion of lymphocytes and an extensive hyperplasia of cells with eosinophilic cytoplasm and large vesicular nuclei. These cells exhibited marked pleomorphism, varying from large round or polyhedral forms to spindle-shaped elements with long protoplasmic projections. Their nuclei were round, oval or crescentic and usually eccentric, and generally contained small chromatin

Fig. 6.—Microscopic appearance of a specimen of xanthoma.

granules. Occasional mitotic figures were present, and many of the cells were actively phagocytic, with erythrocytes, lymphocytes or hemosiderin in their cytoplasm. Occasional cells contained small vacuoles. These cells had proliferated diffusely through both pulp and follicles, and also formed frequent tubercle or rosette-like aggregates in which the cellular elements were elongated and radiated outward from the center of the nodule. The endothelium of many of the sinuses was normal, but in some of the sinuses an occasional endothelial cell contained a mitotic figure, and large round cells, completely or partially attached to the wall, projected into the lumen. The sinuses were filled with groups of similar large cells. Scattered through the pulp were numerous small hemorrhages. With

scarlet red only occasional cells showed small fat or lipoid droplets in their cytoplasm, and no doubly refractive bodies were found. In some of the trabeculae the connective tissue was slightly increased, with an accompanying infiltration of large mononuclear and small round cells, and in a few of the large veins there was an extensive subintimal infiltration of similar cells. Attached to the capsule was a wide band of dense collagenous connective tissue in which were many polymorphous mononuclear and multinucleated cells.

The lymphoid follicles were absent, and the lymph cords were atrophic. Among the lymphocytes in the cords were relatively numerous mononuclear, acidophilic cells, similar to those in the spleen. The sinuses were wide and filled with large mononuclear and multinucleated phagocytes, heavily laden with red blood corpuscles, lymphocytes and polymorphonuclear cells. Numerous rosettes of cells similar to those found in the spleen were present. A few of the phagocytic cells contained cytoplasmic vacuoles. In addition to the phagocytes, numerous erythrocytes and small numbers of neutrophilic leukocytes occurred in the sinuses. Scarlet red demonstrated in some of the large cells in the lymph cords small droplets of fat or lipoid. No doubly refractive bodies were present.

Most of the liver cells were filled with large and small fat vacuoles. Many of the Kupffer cells were swollen, and in the sinusoids were large cells similar in form to the endothelial cells. Some of these were in the process of mitosis, while others had ingested erythrocytes. Collagenous connective tissue in the periportal areas was slightly increased, with small collections of large mononuclear and spindle-shaped cells between the collagen fibers. At the periphery of the portal spaces were small, newly formed bile ducts.

The normal thymic structures had disappeared. In some areas were accumulations of eosinophilic, polymorphous cells similar to those in the spleen. One of the most striking features, however, was the massive collection of huge, vacuolated mononuclear cells with small, deeply stained, centrally placed nuclei—the so-called foam cells—held together by a delicate reticulum. Transitional stages from the smaller acidophilic cells to the large foam cells were found in increasing vacuolation of the cytoplasm of the smaller cells. Multinucleated giant cells with and without cytoplasmic vacuoles were present. In a necrotic mass of cells lay the boat-shaped clefts of cholesterol crystals. About the margins of the accumulations of foam cells, spindle-shaped cells increased in numbers, collagen fibers and capillaries became more numerous, and there was an infiltration with lymphocytes and plasma cells. In other regions there appeared widespread areas of dense, collagenous connective tissue in which a few cells remained. In scarlet red preparations abundant fat or lipoid droplets, many of which were doubly refractive, were demonstrated in the foam cells as well as in many of the elongated cells.

Into the adipose tissue and striated muscle bundles about the thymic mass mononuclear and foam cells, following the interstitial tissue, were penetrating in large numbers, with a gradual replacement of the normal tissue cells.

The pleura was replaced by a thick layer of granulomatous tissue, in the interstices of which were many large mononuclear cells and a few foam cells. The connective tissue in the interlobular septums and about the bronchi and vessels was greatly increased, slightly or heavily infiltrated with large mononuclear cells and lymphocytes, and in the parenchyma of the lung were large fibrotic or fibrocellular nodules. At the periphery of the latter lymphocytic accumulations occurred, and the walls of the adjoining alveoli were widened by infiltrating small round and large mononuclear cells. The compressed alveoli were lined with cuboidal epithelium, and in a few alveolar spaces were small collections of large mononuclear

and polynuclear cells. Many of the cells in the pleurocellular and fibrocellular nodules in the lung contained droplets which retained scarlet red.

A section from the femur revealed extreme changes in both the marrow and the cortex. In the former was a widespread hyperplasia of pleomorphic acidophilic cells similar to those in the spleen; giant and foam cells were numerous, and there were large areas of closely packed spindle cells held together by a heavy fibrillar network, sparsely infiltrated with lymphocytes. This cellular tissue extended into and widely involved the cortex, following and markedly widening the haversian canals, with atrophy of the bony trabeculae. In places the inner half of the cortex was almost completely replaced by the xanthomatous growth (fig. 3).

Essentially similar pictures were found in sections from the right supra-orbital plate, the right mastoid, the parietal bone and both temporal bones. Between both auditory nerves and the bony walls of the internal auditory meati were layers of foam cells, though the nerves themselves were not infiltrated by them. In the vertebrae occasional foci of large eosinophilic cells replaced the normal elements of the marrow. The microscopic changes in the rib were similar to those in the femur, with xanthomatous infiltration of the subperiosteal bone and periosteum. Sections from the sphenoid and sella turcica showed almost entire replacement of the bone by granulomatous tissue, except for a narrow shell of cortical bone and small trabeculae embedded in the granulomatous process. No osseous tissue was found in the floor of the anterior part of the sella turcica, and the xanthomatous mass in the body of the sphenoid was continuous with dense collagenous connective tissue and xanthomatous tissue that filled the sella and surrounded the pituitary. The anterior lobe of the hypophysis and the pars intermedia were normal. The normal architecture of the posterior lobe was almost obliterated by large numbers of polymorphous and spindle-shaped cells. Sections from the infundibulum showed that the thickening of the stalk, observed grossly, was due to the granulomatous process.

In the dura were great numbers of large foam cells, many containing from six to ten or more nuclei, and there were in addition pleomorphic acidophilic cells and areas of granulomatous tissue. Many doubly refractive bodies were demonstrable.

Numerous papillae of the corium were widened by accumulations of large cells with pale vesicular nuclei and abundant eosinophilic cytoplasm and small numbers of lymphocytes. Small hemorrhages had occurred in the regions of cellular infiltration. The epidermis over most of the papillae was intact. In some areas, however, the cellular infiltration was more extensive, involving both the pars papillaris and the pars reticularis, and there was widespread necrosis of the overlying epidermis and the superficial portion of the corium. In the necrotic cell débris erythrocytes and masses of bacteria were entangled. Among the cells infiltrating the corium only an occasional one contained fat or lipoid droplets when stained with scarlet red.

An increase in collagenous connective tissue in which lay large mononuclear and elongated cells and small numbers of lymphocytes thickened the interlobular septums slightly.

The solitary follicles of the intestine, except for a depletion in the number of lymphocytes, were unchanged. In the submucosa were scattered large mononuclear cells.

In the subepicardial fat of the right auricle, covered by epicardium, was a mass of foam and spindle cells with giant cells among them.

In the adipose tissue about the renal pelves and in the perisuprarenal fat were accumulations of cells, varying from the large eosinophilic, nonvacuolated cell to the foam and spindle cell. These were penetrating between the fat cells and replacing the cells of the fat lobules. Among them were many multinucleated giant cells. Moderate numbers of lymphocytes and plasma cells were also present.